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TABLE OF CONTENTS

Further Experiences in the Treatment of Phenylketonuria ALAN MONCRIEFF, M.D., F.R.C.P., F.R.C.O.G., and R. H. WILKINSON, M.D. 763
Results of Treatment in Phenylketonuria STEPHEN COATES, M.A. 767
Phenylketonuria: City of Birmingham Screening Survey MARY M. M. BOYD, M.B., M.SC., M.R.C.P.E., D.P.H. 771
Clinical Features of Intralobar Sequestration of Lung A. W. T. EADE, M.B., and T. B. STRETTON, M.B., M.R.C.P. 774
The Prevalence of Anaemia in the Community G. S. KILPATRICK, M.D., M.R.C.P.Ed., and R. M. HARDISTY, M.D., M.R.C.P. 778
Haematological Findings in Non-white Sick Children in Capetown PHILIP LANZKOWSKY, M.D., D.C.H. 783
Urinary Tract Infection D. J. O'SULLIVAN, M.B., M.R.C.P., M. G. FITZGERALD, M.D., M.R.C.P., M. J. MEYNELL, M.D., M.R.C.P., and J. M. MALINS, M.D., F.R.C.P. 786
Varicocele: A Treatable Cause of Subfertility L. STUART SCOTT, M.D., Ch.M., F.R.C.S.Ed., F.R.F.P.S. 788
Comparison of Subjective and Objective Assessment of Angina Pectoris J. R. A. MITCHELL, M.B., M.R.C.P. 791
Clinical Evaluation of Pheniprazine in Angina Pectoris GERALD SANDLER, M.D., M.R.C.P. 792

PRELIMINARY COMMUNICATIONS

Clinical Assessment of "Etrynit" for Angina Pectoris. E. SOWTON, M.B., M.R.C.P., and S. ORAM, M.D., F.R.C.P. ..794

MEDICAL MEMORANDA

Rupture of Pregnancy in a Rudimentary Uterine Horn. A. P. BARTER, M.B., D.Obst.R.C.O.G. 796

BOOK REVIEWS 797

NEW ZEALAND MEETING

The Scientific Sections 813-20

GENERAL ARTICLES AND NEWS

The Work of a Nurse Employed in a General Practice. ANN CARTWRIGHT, B.SC., and R. SCOTT, M.D., D.P.H. 807
National Association for Mental Health 820
To-day's Drugs 821
OBITUARY 831
MEDICAL NOTES IN PARLIAMENT 835
VITAL STATISTICS 836
MEDICAL NEWS 838
BIRTHS, MARRIAGES, AND DEATHS 840
QUESTIONS AND COMMENTS 841

MEDICO-LEGAL

Negligent Psychiatric Treatment 835
Lady Hoare and the London Clinic 836

LEADING ARTICLES

Varicocele 801
Ménière's Disease 802
The Fleming Memorial 803

ANNOTATIONS

Cysticercosis 804
Micturition Syncope 805
Unusual Inflammatory Reactions of the Eye 805
Mammary Souffle 806

CORRESPONDENCE

Corticosteroids and Dermatological Diagnosis. F. F. HELLIER, F.R.C.P. 821
National Epidemiology. M. A. HEILSMAN, M.R.C.S., D.P.H.; R. J. F. H. PINSENT, M.D. 821

SUPPLEMENT

Full Contents on First Page of Supplement
Annual Clinical Meeting, Canterbury: Programme 89
Science Committee 93
Private Practice Committee 94
Correspondence:
B.M.A. Subscription. F. J. G. LISHMAN, M.D. 96
Public Health Salaries. J. W. R. HAY, M.D. 96
Retrospective Payments for Hospital Medical Staff. C. C. BOWLBY, M.B. ..97

CORRESPONDENCE—*contd.*

Kwashiorkor. C. J. F. BLUMENTHAL, M.S., D.O.M.S.; A. STEPHEN, D.P.H. 822
Tooth Reimplantation. PHILIP COLE, M.D. 823
Spontaneous Rupture of Umbilical Hernia. EDWARD H. WYATT, M.B. 823
Phenylbutazone and Leukaemia. R. SCHEUER-KARPIN, M.D. 823
Oral Treatment of Diabetes. JOSEPH B. HERMAN, M.D., and W. P. U. JACKSON, M.D. 823
Longevity of Haemophiliacs. F. NOUR-ELDIN, M.B., PH.D. 824
Vagotomy for Peptic Ulcer. R. L. HOLT, F.R.C.S.; J. A. D. J. CUNNINGHAM, F.R.C.S.I. 824
Phenazocine and Respiratory Depression. RONALD SHAW, F.F.A. R.C.S. 825
John Hunter on Artificial Respiration. A. E. NICHOLLS, M.R.C.S. 825
Medicine in North America. J. M. THOMAS, M.B., and ERIC COOPER, M.B. 826
Anglo-American Medical Society. A. J. EDEN 826
Myxoedema with Elephantiasis of Eyelids. JACK D. NOYES, M.D. 826
Depression. G. SIMPSON, M.D.; M. B. FELDMAN, D.P.M. 826
Alcoholic Content of Drinks. GUY BOUSFIELD, M.D. 827
Brucella Puzzles. H. R. E. WALLIS, M.D. 827

Letters on other subjects on pp. 828-30

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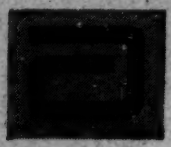

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BRITISH MEDICAL JOURNAL

LONDON SATURDAY MARCH 18 1961

FURTHER EXPERIENCES IN THE TREATMENT OF PHENYLKETONURIA

BY

ALAN MONCRIEFF, C.B.E., M.D., F.R.C.P., F.R.C.O.G., J.P.

AND

R. H. WILKINSON,* M.D.

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Since the last paper from the group at the Hospital for Sick Children, Great Ormond Street, was published (Woolf *et al.*, 1958), further experience has been gained. The patient on whom they reported (their Case 1), and who has an unaffected twin, continues to make good progress and has gone to an ordinary primary school with the twin sister. (The affected twin, born in February, 1955, gave a positive test for phenylpyruvic acid in the urine on the seventeenth day of life, and the special diet was started shortly after her admission to hospital at the age of 3 weeks.) Her I.Q. remains in the mid-eighties, whereas her sister scores over 100. Seen together there seems little to choose between them, except the interesting point that the *affected* child is in fact a little taller and heavier than her normal sister, and her hair is darker. She takes her special food to school. This has been made possible through the closest co-operation by the education authority. She is also lucky in having an intelligent mother.

Low-phenylalanine Diet

At the time of the appearance of the above report on the Great Ormond Street series, a pessimistic comment appeared in the *British Medical Journal* (1958) in which it was stated: "It seems unfortunately to be the case that by the time phenylpyruvic amentia is established a low-phenylalanine diet is likely to raise a child's mental rating only from idiot to imbecile level." Early testing of the urine, now being carried out in many areas as a routine procedure, makes it possible to start treatment at an early stage. Even if diagnosis is made later, the situation is not always so hopeless as is implied by the quotation. For example, here is a summary of a case quoted in replying to the *British Medical Journal* comment (Moncrieff, 1958).

A boy aged 9 months had been attending the Hospital for Sick Children for eczema, and was referred because of backwardness. He was found to be a case of phenylketonuria. Our colleague, Mr. Stephen Coates, made his G.Q. on the Griffiths scale only 30 with a wide scatter—almost at the idiot level. The child was in hospital for six weeks to establish treatment, and then managed continuously and successfully at home. Six months after discharge his G.Q. was 55, and at the age of 2½ years it had reached 64, with some indication of levelling out at this point. He should be able to attend a school for the educationally subnormal.

Horner and Streamer (1959) reported the cases of three children in the United States of America treated from early infancy. After 3½, 2½, and 1 year respectively "the patterns of mental and motor activity are considered to be normal." Hsia *et al.* (1958) in Boston, however, also took a pessimistic line in their report, but their patients were mostly older subjects, and even they admitted possible beneficial effects in four young patients. Blainey and Gulliford (1956) reported clear evidence in two Birmingham patients of acceleration in the rate of development as shown by mental testing, although in one this was not maintained owing to inadequate dietary control at home.

Even if the intelligence is not raised to a satisfactory level the affected children on a low-phenylalanine diet are much more manageable, losing a troublesome restlessness. Fits, if present, cease and eczema clears up. Many parents have asked to be allowed to continue treatment even when it was clear that little or no success was being obtained in raising the intelligence level.

Early Detection and its Difficulties

However, it must in fairness be stated that spectacularly good results are not yet generally found when treatment is started after early infancy, but better results are hoped for those infants in whom the phenylketonuria is discovered at a very early date and treatment is instituted at once. In certain of the older children—for example, detected in the second year of life because of backwardness—there may be a rise of the general intelligence level from, say, 30 to 45, and there the improvement ends. In one case—that of a child with a very conscientious mother and without any evidence of relapse because of failure in giving the special diet—the intelligence level, which had risen to 45, actually dropped back under treatment over the last few years and is now stationary at 30. Similar and even greater and more accelerated falls in the I.Q. have occurred when the special diet has been stopped. One feature of the I.Q. levels which is difficult to explain is that there is a wide variation in the initial level found in children of approximately the same age. There is no clear connexion between the degree of mental retardation and the level of phenylalanine in the blood at the time of examination.

Perhaps not enough attention has yet been paid to the time of taking blood for examination in relation to meals and possible variations throughout the day in

*Now at the Radcliffe Infirmary, Oxford.

the untreated child. The effect of infection and fever on blood levels of phenylalanine was strikingly shown recently in the following case:

A boy aged 3 years had been diagnosed at the age of 14 months and a low-phenylalanine diet instituted and maintained. He had good parents and his blood phenylalanine level had been on the whole satisfactory. He was admitted to hospital for reassessment and partly for social reasons. The urine was negative for phenylpyruvic acid and the blood level for phenylalanine was satisfactory. After a week he developed tonsillitis and fever. Phenylpyruvic acid appeared in the urine and the level of phenylalanine in the blood rose to 15 mg./100 ml. No change was made in his diet, and after a few days the blood and urine reverted to normal.

It may, however, even be that, as in cretinism, there is more than one genetic fault present. It is well recognized that some cretins, diagnosed early and treated successfully as judged by physical standards, fail to achieve a corresponding standard in their mental rating. But as in cretins treatment must be attempted, so in phenylketonurics there is as yet no means of ascertaining whether or not treatment is likely to be successful unless it is tried. Some criteria in this respect were discussed in our last report (Woolf *et al.*, 1958).

Early detection and treatment have presented certain special difficulties. *False negatives* may arise when the urine is not fresh, especially when it has been allowed to stand in a warm atmosphere, since phenylpyruvic acid is easily destroyed. A little chlorbutol or merthiolate should be placed in the specimen bottle to act as a preservative and the specimen kept as cool as possible. The urine should not be acidified if the ferric chloride test is used. When "phenistix" test strips are used they must be quickly dipped in and out of the urine, for the reagents are leached out after a second or two (Gibbs and Woolf, 1959). When there is already an affected subject in a family, the urine of a new baby must be tested frequently in the first six weeks of life before it can be assumed that this child is clear of the disorder. (Serum phenylalanine should also be estimated in all cases of doubt.) Clearly it is a more serious error to achieve a false negative in testing for possible phenylketonuria than the opposite. *False positives* certainly occur, and Gibbs and Woolf (1959) give a valuable list of the sort of reactions found with ferric chloride and with "phenistix" when various substances were added to normal urine. Hudson and Ireland (1959) have also discussed certain aspects of fallacies in the testing for phenylketonuria. Anyone planning a programme for routine testing of the urines of infants should study these two papers carefully.

We see no reason at present to depart from the original conclusion made by our group that a routine test at 3 weeks is the best programme except for babies born into a family in which the possibility of phenylketonuria is present—for example, affected sibs or other relatives. Only a very small proportion of infants with phenylketonuria give a positive test until after the third week, and the administrative difficulties of a double test at present appear to outweigh the advantages.

Dietetic Problems

The "treatment" of young babies presents problems concerned with maintaining growth on a low-phenylalanine diet. The twin referred to above had a stormy passage in the early months, but no special alterations were made to the standard diet and it was maintained throughout. She is now, as already stated, slightly ahead physically of the twin sister. But in a subsequent case the troubles were more serious, and we have been in correspondence with Professor D. B. Macdonald, of Perth, Western Australia, about his difficulties with a young baby.

This child, who had an older affected sibling, was found to develop phenylketonuria at the age of 3 weeks. A low-phenylalanine diet was started, but after 11 weeks there had been no increase in weight. All the necessary supplements (vitamins and minerals) were added with no success, and at the age of 4½ months the child was put on to a whole-milk mixture. There was an immediate gain in weight and the level of phenylalanine in the blood rose and phenylketonuria recurred. After one month the whole milk was gradually reduced and a low-phenylalanine preparation substituted. The blood phenylalanine was reduced to zero and the diet then adjusted to keep this at a low level. The child continued to gain weight satisfactorily and intelligence-testing at the age of 8½ months did not indicate any serious damage, especially in light of the severe physical illness.

A recent experience at Great Ormond Street has also indicated the difficulty of getting satisfactory growth in the early months on a low-phenylalanine diet, and, incidentally, the question of "cure."

A female baby was referred to the Hospital for Sick Children, Great Ormond Street, at the age of 4 weeks because a week previously, on a routine testing of her urine arranged by the local health authorities, a positive reaction to ferric chloride, indicating the presence of phenylketones, had been obtained. This test, by the health visitor, was confirmed on two subsequent occasions by an assistant county medical officer of health. The parents were unrelated, there was no history of any relevant disorder in the family, and there were three elder children of the marriage, one girl and two boys, all normal. The baby had been breast-fed for a few days only and then given dried milk. Her birth weight was 7 lb. (3,175 g.), and on admission at 4 weeks she weighed 8 lb. 13¼ oz. (4,005 g.). Physically she appeared normal in every way. An intelligence test by Mr. Stephen Coates at the age of 6 weeks gave, on the Griffiths mental development scale, a general quotient of 102. Testing of the urine in the ward, with ferric chloride, gave a positive reaction for phenylketone. Laboratory testing gave only a slight colour change with ferric chloride and a negative reaction with the phenistix method. However, the blood phenylalanine level was found to be moderately raised (about 10 mg./100 ml.), and it was decided that at this early age she would probably become worse with more definite reactions in the urine as the phenylalanine in the blood rose.

It was therefore decided to institute dietetic treatment, and after our experience with older children for the most part we placed the baby on a phenylalanine-free diet. At first the feeds were taken fairly well, although the child developed some restlessness. After about a week the phenylalanine level in the blood had decreased but was still raised (about 5 mg./100 ml.). After another week no phenylalanine was detected in the blood. The weight remained stationary. An electroencephalogram at this time (Dr. G. Pampiglione) showed a moderate but definite abnormality, with multifocal discharges of a kind often seen in young patients with phenylketonuria. Milk (2 oz.—57 ml.) was now added daily, but three days later the blood phenylalanine level had risen and the milk was reduced to 1½ oz. (42.5 ml.). The weight rose slowly, but the child was more restless and vaguely unsatisfactory, and a skin eruption appeared on the chin and cheeks. Three weeks later the blood level of phenylalanine was normal. Extra vitamin B was given intramuscularly and the child was transferred to the hospital's country branch at Tadworth. Extra liver extract resulted in an exacerbation of the skin lesion. The child developed tonsillitis, enlarged cervical glands, and some areas of bronchiolitis.

A visiting medical officer thought the skin lesions resembled those of porphyria, and they were now more

extensive. The blood showed a raised phenylalanine level again and the vitamin intake was carefully revised; the question of whether or not the rash could be due to phenobarbitone was raised. There was some regurgitation of watery fluid and a slight increase in the looseness of the stools. There had been virtually no gain in weight for three weeks, and the child was returned to Great Ormond Street. The blood phenylalanine level was still raised and the daily milk intake was reduced to 1 oz. (28.5 ml.). The skin lesions were extensive and unusual. Skin swabs showed pyogenic organisms and no thrush (which had been suggested as a cause). One of us (A. M.) thought they resembled lesions he had seen in Africa in severe cases of kwashiorkor, which led to a consideration of the amino-acid content of the diet (see below). Our colleague, Dr. E. J. Moynahan, who helped us considerably in dealing with the skin condition, was also of the same opinion—namely, that the rash was essentially due to animo-acid deficiency.

Meanwhile the weight continued to drop. The phenylalanine level in the blood had again become normal. The child's condition was, however, deteriorating, and it was decided to abandon the low-phenylalanine diet, at any rate for a period. A half-cream dried milk was started and within a few days the improvement was dramatic. The child took the feeds willingly, gained weight, and the skin lesions, which had resisted several varieties of local treatment, cleared within a few days. A week after the diet had been changed the blood phenylalanine level was still normal. A week later it was slightly raised (6 mg./100 ml.), and after a further week it was back to normal. The urine remained free of phenylpyruvic acid. The child, now aged 5 months, was again tested by Mr. Coates, who found a G.Q. of 83. The child was sent home. A fortnight later the baby had gained over 1 lb. (450 g.) since discharge and seemed flourishing. A month later, now going on to a mixed diet, she had a normal phenylalanine level in the blood, and the urine amino-acid pattern was reported as at the top limit of normal. Further examinations were as follows: April 11, 1960 (aged 10 months): Blood, normal level of phenylalanine; urine, no phenylpyruvic acid, June 2 (aged nearly 1 year): Blood, phenylalanine level, 4.7 mg./100 ml. (this was performed by a new method—L-amino-acid oxidase (Wilkinson, 1961)—in which the normal is 2 mg./100 ml.); urine, no phenylpyruvic acid.

A second electroencephalogram (Dr. G. Pampiglione) showed some improvement on the previous record made at the age of 3 months, but was still abnormal. A third intelligence test (Mr. S. Coates) gave a G.Q. of 103, so that she had regained her original level. It was decided at this stage to keep her on ordinary food and watch her progress, especially as regards her blood phenylalanine level. At 14 months the blood phenylalanine level was normal and she weighed 24 lb. (10.9 kg.).

Comparison of Amino-acid Composition of Diets and Breast Milk (Figures Indicate mg./100 ml., as the "L" Form, which is Either Found or Calculated)

Amino-acid	Hydrolysed Casein Low-phenylalanine Diets		Synthetic Amino-acid Diets (Kwashiorkor) (Hansen *et al.*, 1956)		Human Breast Milk (Clements, 1956)	Bovine Serum Product §
	1 Berry *et al.* (1958)	2 Minafen‡	3 950 mg.	4 1,300 mg.	5 900 mg.	6 1,200 mg.
Aspartic acid	100		66	91	62	135
*Threonine	70	100	39	54	38	89
Serine	110		36	50	43	89
Proline	200		83	114	56	78
Glutamic acid	288		179	247	150	147
Glycine	80		17	24		60
Alanine	94		33	45	20	73
*Valine	140	120	58	80	41	89
*Methionine	10	40	13	18	18	14
Isoleucine	174	100	62	86	47	34
*Leucine		160	92	127	128	101
†Tyrosine	Added	Added (100)	50	69	45	91
*Phenylalanine	Trace	Trace	32	44	47	Trace
*Lysine	170	200	91	125	54	110
*Histidine	5	20	28	39	17	30
*Arginine	28	40	42	58	37	66
*Tryptophan	Added	Added (25)	12	16	17	13
Cystine	5	2	8	11		

* Normally essential amino-acids.
† Probably becomes essential in phenylketonuria.
‡ Data on "minafen" supplied by the manufacturers, Allen & Hanburys Ltd., London.
§ Data on "albumaid XP" supplied by the manufacturers, Powell & Scholefield Ltd., Liverpool.

Supplements to Diet

Since the rearing of young infants who have an impaired tolerance for phenylalanine has been difficult in some instances, it is clear that a careful review is required of the detailed composition of the diet and the supplements supplied during the rapid growth period of the first few months of life. The normal baby doubles its birth weight in five months, and relatively small deficiencies in essential amino-acids and vitamins may produce defects in growth at this age and not necessarily later on. We are at present reviewing the situation with special reference to vitamin-B supplements. The source of amino-acids in the diet is casein hydrolysate that has had phenylalanine removed as completely as possible. Tyrosine and tryptophan, which are removed at the same time, have to be replaced.

The accompanying Table shows two casein hydrolysate diets (columns 1 and 2) and an average breast milk (column 5). The figures for the amino-acid composition are either those found as the L form or calculated in part where the D and L forms were present. Each diet has been adjusted to contain between 900 and 1,300 mg. of amino-acids per 100 ml., as would be found in breast milk appropriate for the age of the infants under consideration. Columns 3 and 4 show figures for the synthetic mixture of amino-acids used by Hansen *et al.* (1956) in the treatment of kwashiorkor. Column 6 shows the analysis of an alternative source of low-phenylalanine diet—hydrolysed bovine serum protein. Apart from the phenylalanine content,* the amino-acid composition of these various diets does not suggest that any important differences are present. The possible use of a low-phenylalanine product other than casein is being explored and the questions of palatableness and cost need careful scrutiny.

The unusual infant whose case is described above failed to thrive, had a marked skin lesion, and was seriously ill on the low-phenylalanine casein hydrolysate diet. It recovered rapidly when a half-cream dried milk was substituted. The low-phenylalanine diet has been adequate for the growth of most of the affected infants. The phenylalanine content of the diet is adjusted by the addition of milk so that it is just sufficient for growth and yet not too great for the infant's impaired metabolism. Individual variations in amino-acid requirements do occur, and this may be the explanation of the dietary difficulties met with in this infant. The phenylalanine requirements of both normal infants and those showing phenylketonuria have been studied by Snyderman *et al.* (1955) and Paine and Hsia (1957).

Individual variations in requirements may cause difficulties. Thus, Berry *et al.* (1958), when examining the dietary requirements of phenylketonuric children fed on low-phenylalanine casein hydrolysate diets, noted one patient with a tyrosine deficiency which was associated with a raised serum phenylalanine level. The patient became irritable. Raising the tyrosine intake

*Since this paper was written, at Dr. Barbara Clayton's suggestion, we have been looking at the nature of the fat present in the special phenylalanine-free foods available. The type of fat added differs appreciably, and it may be that in the young baby the fatty-acid intake needs careful attention.

reversed these changes. It was suggested that tyrosine had become an essential amino-acid when phenylalanine hydroxylation was deficient and that the raised serum phenylalanine levels were due to tissue-protein breakdown. Methionine deficiency caused amino-aciduria and hyperlipaemia. This was corrected by an increased intake of L-methionine and cystine. Similarly, histidine deficiency was associated with amino-aciduria. The deficiencies appeared in different patients on similar diets.

Points in Amino-acid Metabolism

A further point to be considered is that other abnormal aspects of amino-acid metabolism are also found in children with phenylketonuria, the exact significance of which in relation to mental retardation still requires further investigation. Pare *et al.* (1957, 1958, 1959), in London, have discussed associated disorders of tryptophan metabolism, and there is a growing literature on the subject in the U.S.A. The relationship of this to growth difficulties in early life requires elucidation.

It may be that variations in the present regime will be achieved. Geisler and Ströder (1958) have reported that large quantities of fructose (up to 6 g./kg. body weight) raised phenylalanine tolerance, reducing the phenylketonuria present in a normal diet. We repeated this on two children with phenylketonuria, but failed to find any reduction in blood phenylalanine levels (Moncrieff and Wilkinson, 1960).

Can Dietary Restrictions be Relaxed?

The question of whether or not phenylketonuric subjects will require dietetic treatment for life can be settled only after a much longer period of time. Ethical considerations might forbid a relaxation of diet for a trial period, although in an older subject—for example, after physical growth has ceased or even when it is estimated that brain growth has ceased—a period of six months on a normal diet with careful intellectual assessment followed by a return to a low-phenylalanine diet, if necessary, might be justified. The case referred to previously, where apparent " recovery " has occurred, raised the question of a possible late appearance of the necessary enzyme for the hydroxylation of phenylalanine to tyrosine.

It is the labile fraction of phenylalanine hydroxylase which is absent from the livers of patients showing phenylketonuria. This fraction is absent from the livers of foetal animals, but it has been shown by Kenney and Kretchmer (1959) to appear in the livers of rats one or two days after birth, and to reach adult levels one to ten days later. A few observations suggest that there is a deficiency in the enzyme in the livers of premature infants. Several abnormal situations might occur, therefore, if the development of this enzyme proceeded abnormally in early infancy. The enzyme might be absent from the patient's liver at birth and remain deficient during later life, as is probably the case in infants showing phenylketonuria associated with oligophrenia. The enzyme might be absent or low in concentration at birth and develop to normal levels after a variable time. Such infants should present the picture we have described, and their serum phenylalanine levels should return completely to normal later on normal diets. The enzyme might be low in concentration at birth and remain low for a considerable period.

The liver would be unable to meet the increased need of the early growth period for the phenylalanine–tyrosine conversion, and a phenylketonuria would result. The serum phenylalanine levels would not return to normal while this relative insufficiency of enzyme existed, when the patient was taking a normal diet. Alternatively, the enzyme might be present in normal concentrations in the infant's liver but the energy requirements of the reaction might not be met. Whatever the explanation may be, it is clear that some infants are born with a decreased tolerance for dietary phenylalanine. The serum levels of phenylalanine rise and a phenylketonuria follows. Later the infants can tolerate increasing amounts of phenylalanine in their diet. Another speculation might be on the lines of the development of alternative pathways, so to speak. Claims for the apparent failure of any mental retardation to appear in older subjects after relaxation of diet have not been generally accepted and need confirmation. For that reason they will not be further discussed.

Carriers

The detection of heterozygote carriers of the affected gene in phenylketonurics is clearly of importance in relation to prevention by genetic counselling. Healthy relations of affected children would well merit investigation as regards their phenylalanine tolerance. However, the subject is not without difficulties. A loading dose of phenylalanine is costly (about £7), and the methods of estimating blood phenylalanine levels still show a varying degree of experimental error. When using a specific method for diagnosis or for control of treatment some measure of *local* laboratory accuracy is achieved which is sufficient for these purposes. However, for demonstrating a decreased tolerance for phenylalanine in carriers more accurate methods are required, and further investigation in this aspect of the subject is proceeding.* By present methods the parents of phenylketonurics, with some exceptions, are positive as regards a lowered tolerance, and so are approximately two-thirds of the sibs.

The possibility of the experimental production of phenylketonuria is worthy of mention. Workers at the University of Wisconsin have reported the effect of adding phenylalanine and tyrosine to the normal diet of rats, with a rise in the fasting levels of these substances (Auerbach *et al.*, 1958). Waisman and Wang, at the 1959 annual meeting of the American Pediatric Society, reported further experimental feeding of a similar type in dogs and monkeys. The results in the former appeared to have been disappointing, but in monkeys, as recorded in more detail by Waisman *et al.* (1959), it was possible to produce long and sustained raised phenylalanine plasma levels with the excretion of phenylpyruvic acid in the urine. Tests for motor and discriminatory performance and other psychological investigations are proceeding. A further report on this aspect was given by Waisman and Harlow at the 1960 meeting of the American Pediatric Society, and this will no doubt be published. Suggested inferiority in the " intellectual " development, and in two monkeys major epilepsy with fits at long intervals, developed. This experimentally produced disorder will facilitate metabolic experiments not possible in human subjects.

*We are indebted to Dr. L. I. Woolf for a memorandum on the subject of carriers.

General Conclusions

The experiences of the past few years suggest that early detection of phenylketonuria and treatment of these very young infants offer a reasonable chance of preventing mental retardation. There are certain difficulties about early detection which should be overcome. More troublesome is the fact that the diet of the actively developing young baby may have to be more generous in phenylalanine, even to the extent of exceeding the normal blood level, if the child is to survive and thrive. Why some babies are more difficult than others is not yet clear. The dietetic control must be most closely followed by serial estimations of phenylalanine levels in the blood. Probably the simplest dietary treatment would be to use the available phenylalanine-free casein preparations but to add more milk than is usual (more than the maximum of 3 oz. (85 ml.) daily allowed in older children). Whether or not we should also give more tyrosine and tryptophan is not yet clear. Alternatives to the present casein-hydrolysates might help with the cost of the diet. We should like to know more about the enzyme deficiency present, and experimental work may help here. What everyone working in this field would like to know is whether or not dietetic restrictions can ever be relaxed. Evidence on this may be difficult to get, although it is beginning to accumulate.

We are indebted to our clinical colleagues at the Hospital for Sick Children, Great Ormond Street, for permission to use their cases, and to Dr. Barbara Clayton. Dr. G. Pampiglione has taken electroencephalograms when required, and Mr. Stephen Coates has continued to be of most valuable help with intelligence-testing. Dr. L. I. Woolf, who was a member of our original team, is now in Oxford, but continues to help with advice and criticism. Some of the work was supported by the Research Committee of the Hospital for Sick Children. We also thank numerous other friends and colleagues on both sides of the Atlantic who have supplied references and discussed matters personally.

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RESULTS OF TREATMENT IN PHENYLKETONURIA

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This paper reports on further experience in the dietary treatment of phenylketonuria at The Hospital for Sick Children, and follows the papers by Woolf, Griffiths, and Moncrieff (1955) and Woolf, Griffiths, Moncrieff, Coates, and Dillistone (1958). This experience is considered in the light of a review by Knox (1960), especially our successes and failures in treatment. As Knox gives an evaluation of treatment based on all the treated cases published up to the end of 1959, it is not necessary to review the literature here. The neurological aspects of the patients will be dealt with in a later paper. Moncrieff and Wilkinson (1961) discuss our current views on the biochemistry of the disease, and the present paper is concerned mainly with the psychological aspects.

Material

Up to October, 1960, 35 cases of phenylketonuria have been considered for treatment at The Hospital for Sick Children since the dietary treatment was started in October, 1953. These are listed in Table I. Case 34 has already been the subject of a paper (Coates, Norman, and Woolf, 1957), and Case 35 is mentioned by Moncrieff and Wilkinson (1961). These are not discussed here. Of the remaining 33, two (Cases 32 and 33) have only had their initial test before starting treatment: they will therefore be used only in calculating the level of abilities found before treatment.

Thirty-one cases have been treated and had their second test, but in six of these (Cases 26–31) treatment has been ended for various reasons.

Material from our earlier papers is repeated. The case numbers of the present series and the corresponding numbers in those papers are as follows:

Present Series	1958	1955
Case 1	Case 11	
,, 3	,, 6	
,, 9	,, 3	Case 2
,, 10	,, 2	
,, 20	,, 9	
,, 24	,, 8	
,, 25	,, 1	
,, 26	,, 4	,, 1
,, 28	,, 10	
,, 29	,, 5	,, 3
,, 31	,, 7	

The children are tested for intelligence before treatment starts, then three months later, three months later again, six months later, and then yearly. Originally we tested much more often, but the additional information is no longer useful. The Griffiths mental development scale is used on children with a mental age below 2 years: 75% of 192 tests up to date. The Merrill–Palmer scale and the Revised Stanford–Binet intelligence scale are used for children of higher mental age.

Results of Treatment

The results of treatment are given in Table I. Cases 1 to 25 are still being treated and have had more than one test. They are listed in order of the size of the increase in the intelligence quotient from the initial to the latest test.

Whether or not the final outcome is improvement, the test measures in any one case naturally vary above and below the trend of that particular case. The latest measure used in this paper may therefore not always be the highest, to some extent as a result of chance. The latest score is in fact less than the highest in 10 of these cases. In assessing results the latest measure has been used—therefore making the results slightly less satisfactory—but the highest scores are also given in Table I. It will be seen, from Cases 26, 27, and 28, that a child may temporarily improve and then revert to a measure so close to the original that eventually treatment is stopped. It therefore seemed better to use the latest rather than the highest measure in assessing the effects of the diet.

Case 25 is a special one. Since this patient's elder sister was a known phenylketonuric (Case 20 of this series) the patient was herself diagnosed at 17 days and has been on the diet since she was 4 weeks old. The quotient dropped to 81 after two years, but has since climbed fairly steadily to the latest figure of 94, her present age being 5 years 6 months. We naturally did not expect an improvement in her intelligence, and the loss of 25 points is not important, since the first test would inevitably be unreliable at so early an age. Her normal non-identical twin sister began with a quotient of 113, and on last testing at 4 years of age this had dropped to 108.

Discontinued Cases

Treatment has been stopped, after various periods, in six cases (Nos. 26–31). The latest quotients tabulated are the last before treatment stopped. The reasons for stopping in Cases 26, 28, and 31 have already been stated in our last paper (Woolf *et al.*, 1958). The mother of Case 30 never really tried the diet, as she would not agree that her child was very backward.

Two patients (Cases 27 and 28) showed slight initial improvement, but this was not maintained, the measures finishing at a slightly higher level. In both cases it was difficult to keep the child on the diet and pointless to continue the uneven struggle.

All these children have been tested since stopping the diet, with results (Table II) which may be compared with three cases quoted by Knox (1960) from Armstrong *et al.* (1957).

TABLE I

Case No.	Sex	Initial Quotient	Latest Quotient	Change in Quotient	Highest Quotient if Different from Latest	Age at Initial Test (Weeks)	Period of Treatment (Weeks)	Rate of Improvement*
1	M	36	74	38		118	166	0·23
2	M	57	88	31		70	288	0·14
3	M	29	57	28	65	42	190	0·15
4	M	31	58	27	62	43	119	0·23
5	F	8	31	23		54	214	0·11
6	F	28	48	20	50	69	78	0·26
7	M	41	61	20		47	165	0·12
8	F	47	64	17	72	152	304	0·06
9	F	71	85	14	93	152	295	0·05
10	M	48	60	12		130	132	0·09
11	F	34	46	12		106	77	0·16
12	M	18	27	9		37	109	0·08
13	F	67	71	4		327	30	0·13
14	F	83	87	4		65	42	0·10
15	M	42	45	3		63	70	0·04
16	M	74	77	3		28	28	0·11
17	M	21	23	2	32	63	220	0·01
18	M	38	40	2	41	307	96	0·02
19	F	32	32	0		234	97	
20	F	24	23	−1	31	94	218	
21	M	32	31	−1		68	241	
22	F	49	48	−1		455	95	
23	F	44	39	−5	51	64	163	
24	F	63	56	−7	83	19	216	
25	F	119	94	−25		4	274	
26	M	20	29	9	30	138	142	0·06
27	F	23	31	8	34	124	112	0·07
28	M	20	25	5	34	80	220	0·02
29	F	11	14	3		279	221	0·01
30	F	33	33	0		85	0	
31	F	49	49	0		132	4	
32	M	15				44		
33	M	40				42		
34	M							
35	F							

* The rate of improvement is the rise in quotient per week of treatment, derived by dividing the increase in the quotient by the period of treatment. It is not the same as the progress rate, which is the increase in mental age divided by the increase in chronological age multiplied by 100. It seemed (Woolf *et al.*, 1955) that this latter figure might stay constant for a particular child and enable us to predict the final adult intelligence level, but this has been disproved. The situation is too complex for such simple mathematical predictions, and the rate varies from month to month.

TABLE II

Case No.	Age (Weeks)		Duration of Treatment (Weeks)	Period after Treatment (Weeks)	Intelligence Quotient		
	When Diet Started	When Last Seen			Initial	When Diet Stopped	At Follow-up
26	138	280	142	?	20	29	21
27	124	323	112	87	23	31	21
28	80	356	220	56	20	25	32
29	279	300	221	90	11	14	10
30	85	182	0	97	33	33	30
31	132	278	4	142	49	49	37

It would seem that there are no effects, all the differences being accountable for by chance. Improvement, such as it may be, is not usually maintained, but there is also no appreciable loss of ability.

Organic Psychosis

There are five children (Table III) whose behaviour warrants the diagnosis of autism or juvenile psychosis. They are withdrawn, unable to make a relationship even with their mothers, fairly wild and unmanageable, non-speaking, and given to uttering peculiar noises and displaying many kinds of mannerisms, often of an auto-erotic kind. These are Cases 11, 17, 20, 21, and 27.

TABLE III

Psychotic Cases				Non-psychotic Cases of Comparable Initial Quotient			
Case No.	Initial Quotient	Latest Quotient	Age at Start of Treatment (Weeks)	Case No.	Initial Quotient	Latest Quotient	Age at Start of Treatment (Weeks)
11	34	46	106	3	29	57	42
17	21	23	63	4	31	58	43
20	24	23	94	5	8	31	54
21	32	31	68	6	28	48	69
27	23	31	124	12	18	27	37
				19	32	32	234
				28	20	25	80
Means	27	31	91		24	40	80

They are all of low initial intelligence quotient—the average is 27—but this cannot be held responsible for their condition, since there are seven children of comparable initial intelligence who are not similarly affected (Cases 3, 4, 5, 6, 12, 19, and 28). There is a tendency for the psychotic to have started treatment at a later age than these seven non-psychotic. Five of the seven non-psychotic were treated early (before 70 weeks), whereas only two of the five psychotics were treated so early.

It may be that we have prevented a psychosis in Cases 3, 4, 5, 6, and 12 by starting treatment early, though the fact that we failed to prevent it in Cases 17, 20, and 21 suggests that there may be selective brain damage and that in some children there is an organically induced psychosis as well as an organically caused mental deficiency. That the two conditions are not necessarily

related is shown by Cases 5, 12, 19, and 28, where the final quotient is still very low but the child is clinically by no means psychotic. In some of the psychotic cases the mothers were unable to provide the optimum environment, but this failure, as also their failure to keep the child strictly on the diet, was by no means restricted to these cases. Thus Case 3 has been very poorly handled by a mother preoccupied with her own personal problems, and the child has not always been kept strictly to the diet, but there is no psychosis and there is improvement. It seems that where there is this selective damage to the personality any change in the brain is not accompanied by improvement in the intellect, probably because the intellect cannot improve if the mind is diseased. But when the mind is not diseased, for all that the brain is damaged, as in Case 3, then the intellect can improve.

Rapid Changes

It has happened that in four cases there has been a considerable rise in the quotient between the initial and the second test, and this has led to an overoptimistic prognosis at the time of the second test. These cases are shown in Table IV. There are three other cases

TABLE IV

Case No.	Age at Start (Weeks)	Initial Quotient	Interval between Tests	Second Quotient	Latest Quotient
3	42	29	33 weeks	55	57
4	43	31	16 ,,	59	58
5	54	8	17 ,,	19	31
6	69	28	17 ,,	47	48

(Nos. 7, 15, and 17) of comparable age, initial intelligence, and interval which do not show this sudden jump. Presumably in the "jumping" cases we are seeing the effects of the removal of intoxication from a damaged brain: the immediate effects are dramatic, but the permanent damage is such that complete repair is impossible, and though further permanent damage may be prevented the result is still a child who is considerably retarded intellectually.

Sub-scale Differences

The Griffiths scale consists of five subscales: A, locomotor; B, personal–social; C, hearing and speech; D, eye and hand; and E, performance. In the normal child there will be only slight differences in the scores across these five subscales. Children with specific defects show up early by a relative failure on one subscale. Thus spastic children will fail on the locomotor scale and deaf children on the hearing and speech scale. We investigated discrepancies on 87 tests carried out by 25 of the patients. The major discrepancies are on the locomotor scale and the performance scale. The locomotor scale tends to be the highest of the five on any one testing and the performance scale tends to be the lowest. The three other tests behave in no consistent fashion beyond being between these two extremes. Of the 87 tests, only 21 (24%) showed no discrepancy—that is, neither the locomotor scale, the highest, nor the performance scale, the lowest. On the other hand, 25 (29%) have both a high locomotor and a low performance at the same testing. These discrepancies are much more pronounced in the second year. Thus 15 (33%) of the 45 tests yielding a mental age less than 52 weeks show no discrepancies but only 5 (14%) of the 42 tests yielding a mental age between 52 and 104 weeks. The results of this investigation are shown in Table V. It will be seen that the chances are that three-quarters of all tests on these children will show a discrepancy of either scale A or scale E, and that the possibilities are greater (3:2) that it will be in scale A.

TABLE V

	No. of Tests	Locomotor High	Performance Low	Locomotor High and Performance Low	No Discrepancies
All tests	87	55 (63%)	36 (41%)	25 (29%)	21 (24%)
1st-year tests ..	45	20 (44%)	21 (47%)	11 (24%)	15 (33%)
2nd- ,, ,, ..	42	35 (83%)	15 (36%)	14 (33%)	6 (14%)

It will also be seen that the chances of obtaining a discrepancy are greater in the second year than in the first (9:7). In the first year the discrepancies which will probably occur in 67% of tests will be equally divided between a high locomotor and a low performance score, with a quarter of the cases showing both at once. In the second year the great majority (83%) will have a high locomotor score, but the 36% with a low performance score are probably no more than would be expected by chance.

Two conclusions can be drawn. In the first place it is clear that the locomotor scale alone would be a very inadequate indication of intellectual status in the second year of mental life. Assessments based on locomotor skills—crawling, walking, climbing stairs—will be misleadingly optimistic. Inferences from low performance scale scores may well be unduly pesimistic in some cases, though this scale is most like a normal intelligence test; but these inferences are less likely to be made.

In the second place it is worth noting that the damage to the brain in these children seems not to affect physical development. We do not find paralyses or disturbances of locomotion. In another series of brain-damaged children, hydrocephalics, there is a close correspondence between degree of mental defect and degree of physical handicap (Laurence and Coates, in preparation). It would be interesting to know why a metabolic abnormality which causes irreversible damage to the brain (Crome and Pare, 1960*; Hsia *et al.*, 1958) should selectively be less damaging to locomotor development, relatively speaking, than to the intellect as a whole, while other post-natal diseases of the brain seem to affect intellect and locomotion equally.

Evaluation of Results

In order that our series might be compared with the 43 cases collected by Knox (which included eight cases from our 1958 paper, which are repeated here), our results have also been assembled in Table VI in the form he uses.

It is immediately apparent that the distribution of our untreated cases is very different from that of 466 untreated cases collected by Knox. Presumably our cases are younger and therefore show less deterioration. We do not know the average age of the 466 patients, but they include a large number of adults, whereas our sample consists entirely of children varying in age from 4 weeks to 8 years 9 months, 80% being under 3 years old. It seems quite invalid to compare treated cases with those 466 untreated, since such a comparison would give a falsely optimistic view of the effects of the diet.

We can claim to have had some moderate success from the diet. Table VI shows that, taking all 31 treated

*Crome and Pare (1960) refer in their bibliography to a non-existent paper: Woolf, Griffiths, and Moncrieff, *Brit. med. J.*, 1954, **1**, 1957.

cases (which include 6 whose treatment was ended, two of them never really on diet), the shift in proportions of cases in the various quotient categories is clearly significant. From Table I it can be seen that 22 cases improved (Nos. 1–18 and 26–29). Some of these were only borderline successes (Cases 13–18). Eight cases appear to be failures (Cases 19–24 and 30–31). These failures and borderline failures are discussed in detail.

TABLE VI

Intelligence Quotient	Untreated Cases		Treated Cases (31)		Treated Started Before 3 Years			
	466 (Knox, 1960)	All Our Cases (33)	Before Treatment	After Treatment	Before Treatment (26 Cases)	After Treatment (26 Cases)	Started Before 16 Mths (14 Cases)	Started After 16 Mths (12 Cases)
0–20	64·4	18·2	19·5	3·0	15	0	0	0
21–40	23·2	39·4	35·0	39·0	38	39	36	42·0
41–60	9·7	24·2	26·0	29·4	27	31	36	25·0
61–80	1·9	12·1	13·0	16·0	12	15	14	16·5
81–	0·6	6·1	6·5	12·6	8	15	14	16·5

Failures

In Cases 30 and 31 the failure was clearly attributable to the diet never having been properly tried. They are cases of failure of our treatment of the parents but not necessarily failure of the diet.

The loss of ability in Cases 23 and 24 may not be permanent. It will be seen that both have shown higher quotients in the past. Case 23 went up from 44 to 51 in the course of the first year of treatment, and Case 24 from 63 to 83 over three years. There is no explanation for the subsequent drop to 39 in Case 23. There has been good dietary control and the blood phenylalanine levels have always been satisfactory. The drop in Case 24 is more easily understood, since the diet had not been adhered to, there had been many upheavals in the home, with the mother very disturbed and the child being cared for by different people. The situation is better now. We may see some improvement in both these children, and so we are keeping them on the diet.

Cases 19 and 22 were probably too old to benefit from the diet (234 weeks and 455 weeks), though age is not the only factor, as we shall see below.

Cases 20 and 21 failed apparently because they became psychotic; so that, though they were fairly young (94 and 68 weeks respectively) when they started the diet, the damage to the personality, the organic psychosis, made it impossible for the intellect to improve.

Borderline Cases

Cases 13, 14, and 16 are all high-grade (initial quotients of 67, 83, and 74) and have been on the diet for only short periods (30, 42, and 28 weeks), so that very much change should not be anticipated as yet. Their rates of improvement are all 0.10 or more, so we could hope to get Cases 14 and 16 into the average range of intelligence, since they were young when they started the diet (65 and 28 weeks), but we would not be too optimistic with Case 13, since she is much older (327 weeks: 6 years 3 months). In her case we hope to prevent further deterioration rather than aim for improvement, which is unlikely to continue at the present rate.

Case 18 is another of the psychotic children, and the relative failure here has probably the same causes as in Cases 20 and 21. Case 15 was probably too old.

Dietary Control.—In all these last cases (Nos. 13–24) the dietary control has been satisfactory, so far as we know, except in the cases already mentioned.

Effect of Age

In an earlier paper (Woolf *et al.*, 1958) we suggested the rule that treatment should be tried if the quotient was more than 20 at 2 years, more than 30 at 3 years, and more than 40 at 4 years. In other words, we were clearly of the opinion that as early a start as possible was essential. As a result of his work with Hsia *et al.* (1958) Knox uses 3 years of age at the start of treatment as a point above which improvement is negligible. Our figures are rather too disproportionate to assist in the investigation of this suggestion, since so few of our patients are over 3 years old. The relationship between age and change is shown in Table VII for 28 cases (excluding Nos. 25, 30, and 31), adopting 3 years as a dividing-line.

Therefore, using the criterion of any rise in the quotient between initial and final test (Cases 1–18 and 26–29), 5 out of 7 of those over 3 years (71%) and 17 out of 21 of those under 3 years (81%) improved; or, using the criterion of exclusion of all borderline and terminated cases (Cases 1–12) 2 out of 7 of those over 3 years (29%) and 10 out of 21 of those under 3 years (48%) improved.

It is apparent that better results are obtained in those under 3 years, but 71% of our small number of those over 3 years show some (at times only temporary) improvement, and 29% show quite definite improvement —not a negligible proportion. Our number of cases, however, is so small that these proportions must be treated with caution.

Though these figures suggest that the younger children do better, this is not true for our cases as a whole. Knox obtained a high correlation of -0.67 between the age at the start of treatment and the final quotient, using 43 patients under 3 years of age. Our figures do not give the same result. The correlation on our similar cases—there are 26 cases if we include Case 25—is only -0.08. Even if we include all 31 of our cases there is no correlation between initial age and final quotient ($r = -0.15$).

Table VI suggests that those who started treatment before 16 months did better than those who started later, which would be consistent with the results Knox collected. But this difference is spurious, since the 14 children who started before 16 months and appeared to do better were in fact better to begin with, their average initial quotient being 45, whereas the average of the 12 who started after 16 months was 39.

TABLE VII

Improved	No. of Cases	% of 28	Failed	No. of Cases	% of 28	Totals No. of Cases	Totals % of 28
Over 3 Years							
Quotient rise of 9 or more points	2		No rise or a fall in quotient	2			
Quotient rise of less than 5 points	2						
Quotient rise but case terminated	1						
	5	18		2	7	7	25
Under 3 Years							
Quotient rise of 9 or more points	10		ditto	4			
Quotient rise of less than 5 points	4						
Quotient rise but case terminated	3						
	17	61		4	14	21	75
	22	79		6	21	28	100

By calculating the rate of improvement we have attempted to find out what does influence the result (Table I). Unfortunately, this tells us very little. It is negatively correlated with the age at which treatment was started ($r = -0.32$), meaning that the lower the age the greater the rate of improvement, but the figure is not statistically significant. The rate, which is naturally correlated with the size of change from which it is derived ($r = 0.66$), is not correlated with the initial quotient ($r = 0.11$). It is negatively correlated with the period of treatment (-0.28), but this again is not significant, though one would expect the rate of improvement to slow down as the figure suggests. From our figures it is extremely difficult to say on what the final outcome does depend.

In other words, we would still recommend starting treatment as early as possible. But the fact that it is begun early is no criterion by which to assess how successful the treatment will be. If it is delayed the results are less likely to be good, but they may well be good in about a quarter of the cases.

The explanation may possibly be found in two facts. First, though it may be agreed that 75% of the variation in intelligence between normal people is genetic in origin (Burt and Howard, 1956), it is nevertheless probable that this relationship does not obtain much before the age of 3 or 4 (Skodak and Skeels, 1949; Honzik, 1957), as is also true of the genetically determined proportion of variations in height (Bayley, 1954; Tanner, 1960). If the genetic influence is by no means completely effective before 3 years of age we would, theoretically, not be able to predict intelligence levels within these years. The second fact suggests that this is largely true. Longitudinal studies have shown that predictions based on tests within the first 18 months will be very uncertain—only about 36% correct (Hindley, 1960). With these doubts in mind it is not surprising that the addition of variables—such as degree of biochemical intoxication, degree of detoxication, hospitalization, lowering of intelligence—makes prediction impossible. Some of the children who fail, though treatment was started early, may well have been going to be dull, and were therefore more susceptible to the disease; some who do well, though treatment was started late, may well have been born to be very intelligent, and our pleasure at an I.Q. of 90 may mask the fact that the child may have lost 50 genetic I.Q. points. Probably we can never know in any one case. We can only say that treatment should be tried, and be given up if no improvement of any kind occurs (Moncrieff and Wilkinson, 1961).

The lack of predictive power from infant tests does not in the least lessen their value in this type of work. Without some objective measurement we cannot assess whether any particular child is benefiting from the diet. It may not be valid to compare a child's test score at 12 months with the normal, but we can more validly compare a child with itself and watch for changes in the degree of backwardness. For this purpose the Griffiths scale seems by far the most useful instrument.

Summary

Up to October, 1960, 35 cases of phenylketonuria have been treated at The Hospital for Sick Children since dietary treatment was started in October, 1953; 31 are discussed.

Treatment was terminated in six cases.

One patient (Case 25) born with average intelligence and treated since she was 4 weeks old has retained that level up to 5 years of age.

Of 28 cases in which the diet was given a fair trial, 22 (79%) showed improvement; in 12 (43%) this improvement was marked—a rise in I.Q. of 9 or more points—and appeared to be permanent.

The reasons for the variations in result are discussed; to some extent these variations are attributed to the impossibility of accurate prediction in young babies.

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PHENYLKETONURIA: CITY OF BIRMINGHAM SCREENING SURVEY

BY

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The possibility of the prevention of mental retardation associated with phenylketonuria by early diagnosis and treatment (Blainey and Gulliford, 1956; Woolf *et al.*, 1958; Brimblecombe *et al.*, 1959) has resulted in local health authorities carrying out tests for phenylketonuria on a wide scale. In Birmingham arrangements were made to test every infant born in 1959 and living in the city at the age of 6 weeks. In order to ensure early diagnosis it was planned to carry out the test as soon after that age as possible, and certainly before the age of 3 months, so that treatment by suitable diet could be instituted before cerebral damage occurred.

In an extensive screening survey it is rarely practicable to apply more than one test per infant. Testing at 6 weeks of age was therefore chosen to ensure that no case would be missed because of insufficient excretion of phenylpyruvic acid to give a clear positive test. Baird (1958) suggests that all known phenylketonuric children excrete more than 30 mg. of phenylpyruvic acid per 100 ml. after the age of 34 days.

Methods

Paper strips treated with ferric chloride solution were regarded as the most practical method of testing with over 19,000 predicted births in 1959 in Birmingham. Commercially produced strips (" phenistix ") which gave a clear colour change were made available by the manufacturer.

The collection of fresh urine was regarded as unsatisfactory, especially in view of the failure to test 73.3% of Cardiff infants in a similar scheme because urine samples could not be obtained. Ferric chloride solution dropped on napkins gives a positive reaction (Centerwall, 1957) but leaves an ugly stain which is extremely difficult to remove even with detergents or bleaching agents. Attempts were made to squeeze urine from the napkin and also to test filter paper pressed on to the napkin, but these also were unsuccessful.

Administration

To stimulate the interest and enthusiasm of the staff, a physician interested in phenylketonuria gave lectures illustrated by film sequences of treated and untreated cases. He also demonstrated the methods of testing both with 5% ferric chloride solution dropped into a specimen of urine and with treated paper strips. Positive tests could be examined, as well as the effect of wetting on the appearance of the strip.

A sample of urine from an untreated case was kept available in a refrigerator for health visitors to refresh their memories of positive tests, as most of their tests were negative. Events showed, however, that the comparison of the test-strip with the colour scale on the container was the most useful safeguard against misreading a test.

Testing began in mid-February, 1959, when the first babies born that year reached the age of 6 weeks, and continued until March, 1960, for those born in 1959. Infants born in 1960 are being tested now.

The health visitor who held the infant's home-visiting card was responsible for carrying out the test and recording the result in the appropriate place on the printed record card. If an infant attended a welfare centre in another district the test could be done there and the result sent to the responsible health visitor on a duplicated slip. The result was also prominently marked on the infant's medical notes at the centre.

The health visitors were advised to avoid mentioning mental defect to the parents, and to treat the test as a routine matter. For mothers who required a more detailed explanation it was recommended that they be told that the test was to exclude the presence of rare inborn errors of metabolism.

The health visitors were provided with bottles of phenistix and wooden spatulas. The prepared end of the " stick " was placed between folds of a freshly wet napkin and pressed on with a clean wooden spatula. The strip was removed after about 30 seconds and compared with the colour chart on the bottle. In the event of the health visitor obtaining a positive or doubtful result a specimen of urine was obtained and tested with ferric chloride in a test-tube. The medical officer dealing with the administration of the survey was also informed as soon as possible. Any infants not tested by the age of 3 months and any refusals by parents to permit the test were also reported. A few infants who had long spells in hospital, and a few whose parents refused a test, comprised the very small group not tested by the age of 3 months. The urine of infants still in mother and baby homes in the city at the age of 6 weeks, and those in care in children's homes, was tested there by the matrons and the results were returned each month to the office, where the home visiting cards were retained, for recording. In these cases it was possible to obtain specimens of urine, and these were tested in test-tubes with 5% ferric chloride solution. None of these 200 tests were positive and no difficulty arose with false positives due to *p*-hydroxyphenylpyruvic acid (Gibbs and Woolf, 1959).

Arrangements were made for the examination of the urine of any positive cases by paper chromatography in the University Department of Experimental Pathology before the child's parents were informed of the need for the child to see his doctor. After confirmation of a positive result the child's general practitioner was informed and advised on existing special facilities for treatment at an appropriate hospital out-patient department.

Some difficulties were encountered by the health visitors in attempting to do the test. The routine first visit, usually paid as soon as possible after the midwife ceases to attend, or after the discharge of the mother and baby from hospital, was too early to be sure of a positive result in all cases of phenylketonuria. A special visit had therefore to be paid if the mother did not bring her baby to a welfare clinic. The napkin was often dry or the infant asleep on the occasion of a visit, so that several visits were sometimes necessary to secure an opportunity of testing. Co-operative mothers were asked to keep the napkin removed at the time of the 2 p.m. feed in a plastic bag on a day arranged by the health visitor to visit, or to bring it to the clinic early on the same afternoon. The visiting involved in securing comprehensive screening is considerable, since 69% of infants born in 1959 attended infant welfare centres in 1959, and an estimated 74% would have attended in Birmingham up to March, 1960. Over 26% of infants must therefore be tested in their homes, as they will not attend a centre before 3 months of age. It speaks well for the relationship of the health visitors with the mothers that only 35 parents (0.18%) refused to allow the test. One of these was a dentist, another a general practitioner, while some others in social classes IV and V refused all dealing with health visitors and infant welfare centres.

Table of Results

No. of children born in 1959 in Birmingham County Borough		19,353
" " " and tested at 6 weeks of age or over		18,981
" No. of negative results	18,977	
" " positive " results (including one proved case of phenylketonuria)	4	
No. of refusals to permit test		35
		19,016
No. of children who left the city before the test was due or could be carried out		417
Neonatal deaths and infant deaths before the test was due or could be carried out		379
		796
Total		19,812

Infants born in 1959 outside the city and entering it account for the total number being in excess of the number of births in the city.

Discussion

Of the four " positive " tests recorded, three were weak positives corresponding with the palest colour change on the chart (less than 15 mg. of phenylpyruvic acid per 100 ml.). The urine of the fourth, which proved

to be a case of phenylketonuria, was negative on testing in a maternity hospital at the age of 2 weeks but positive at 6 weeks.

A urine sample from the first child showing a weak positive reaction proved negative on testing with 5% ferric chloride solution. There was no suggestion of errors of technique on the part of the health visitor, nor was she colour-blind to Ishihara tests. Subsequent specimens of urine were intermittently very weakly positive with phenistix and with ferric chloride. Paper chromatography of the urine showed that this baby intermittently excreted small quantities of phenylalanine in the urine, although never as much as in cases of phenylketonuria. The baby continued to develop normally and has been carefully followed up to observe her progress. Both her parents are Irish and she has no relatives known to be suffering from mental disorder.

The second weak positive found was similar to the first. A specimen of urine collected on the same day gave no reaction with ferric chloride. A chromatogram of the urine procured a few days later showed a trace of phenylalanine, but no phenylpyruvic acid. The baby was developing normally and was first tested at 8 months of age, when she came to live in Birmingham. A second chromatogram on a specimen of the urine collected three months later was entirely normal.

From the other weak positive to phenistix, again showing barely a 15-mg. colour change, no specimen has so far been procured.

The question arises whether these weak infant excreters are heterozygotes, who may produce children with phenylketonuria if they marry partners like themselves. At present the only way to demonstrate the heterozygous "carrier" is to measure the effect of a large oral dose of phenylalanine on plasma phenylalanine levels (Hsia *et al.*, 1956). Adult relatives of phenylketonurics do not excrete sufficient phenylpyruvic acid to give even a weak positive test. It is not possible to obtain blood for phenylalanine estimations from healthy infants without lengthy and possibly frightening explanations to parents and is unjustified when no benefit to the child will accrue. Some parents are "clinic-shy" and require very tactful approach from health visitors to procure a minimum of co-operation. The suggestion is compatible with the finding that in heterozygotes the fasting blood level of phenylalanine is higher than in a normal group (Hsia *et al.*, 1956; Berry *et al.*, 1957; Knox and Messinger, 1958).

False-negative results from phenistix may be due to placing the test strip in a dry napkin and reading the result when the napkin is next changed, by which time a positive reaction may have faded; to dropping the test strip into a sample of urine, when a colour change may not be noticed because the reagents are bleached out of the strip; or to pressing the wet napkin on to the test strip too firmly and for too long, when the chemicals may drain from the strip and the colour change be missed (Hudson and Ireland, 1959; Gibbs and Woolf, 1959). When specimens of urine could be procured testing with 5% ferric chloride prevented one of these possibilities of error and the directions to the health visitors avoided the others.

In association with this survey of 1959 babies, a case of phenylketonuria in a child then aged nearly 4 years was found. Repeated attempts to obtain a specimen of urine at the clinic had been unsuccessful, and, as the boy had been seen at a hospital out-patient department at the age of 2 on account of his mental retardation the health visitor had not worried the mother about it. The health visitor, however, tested the child's napkin on a routine visit to the home and found it strongly positive. The child is now under treatment. His brother, aged 10 months, whose urine was negative to phenistix and ferric chloride, also had a chromatogram of a single specimen of his urine and was found to be excreting very small quantities of an unusually large number of amino-acids, but no phenylalanine. The napkin of another child aged 2 was tested with phenistix because he was backward and had just come to live in Birmingham. It was found to be very weakly positive, but a specimen of urine passed three days later was negative both to phenistix and to ferric chloride, and chromatography proved normal. His mental retardation could not be attributed to phenylketonuria. His mother is thought to be below average in intelligence.

Summary

The organization of a screening survey for phenylketonuria covering 98.8% of infants born in 1959 and living in a county borough at 6 weeks of age is described.

The results are tabulated and demonstrate that testing of the freshly wet napkin with phenistix is a practicable method for the comprehensive screening of young infants.

Correct use of phenistix is important.

The incidence of cases is that expected—namely, about 1 in 20,000.

The occurrence of intermittent very weak positive tests in an infant whose development apparently proceeded normally is recorded.

Intermittent true but very weak positive tests may recur in children who develop normally.

I thank Dr. Matthew Burn for permission to publish this paper and for his advice, and Dr. E. L. M. Miller for advice and help. I am indebted to Dr. J. D. Blainey for the results of the chromatograms and also for constant advice and for reading this paper. My thanks are also due to Miss Milner and the health-visiting staff of the City of Birmingham for their co-operation.

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The late Professor J. Cameron, whose obituary was published in the *Journal* of December 31, 1960 (p. 1959), directed his trustees to give the two gold medals "which I gained at Edinburgh University to the Bank of England for the purpose of being added to the gold reserve of Great Britain." He also directed that the illuminated souvenir of the banquet "given to me in the Lord Nelson Hotel, Halifax, Nova Scotia, Canada, in 1947 by former students and friends, containing the signatures of 108 hosts, be placed in the John Cameron Rooms, Forrest Building, Halifax, Nova Scotia, so that succeeding generations of students may be enabled to see the signatures of their forefathers."—*Glasgow Herald*, February 16.

CLINICAL FEATURES OF INTRALOBAR SEQUESTRATION OF LUNG

BY

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Intralobar bronchopulmonary sequestration is a condition that has received general recognition only in the past decade.

The lesion is congenital in origin and consists of a portion of lung which is not in communication with the main bronchial tree and is supplied by an artery other than the pulmonary artery This vessel usually arises from the lower thoracic or upper abdominal aorta, and passes, directly or through the diaphragm, to the sequestrated lung; it is elastic in type and often undergoes atheromatous change. The segment itself usually lies in the postero-medial part of one or other lower lobe. The mass is usually cystic, with evidence of bronchial structures in the cyst walls, shows inflammatory changes, and is devoid of visible carbon pigmentation.

Such segments are peculiarly liable to infection, and in the past have usually come to light as a result of recurrent pulmonary sepsis, although the correct diagnosis has often not been apparent until the aberrant artery has been discovered at operation. It is now evident that features exist which allow a strong presumptive diagnosis to be made even when recurrent infections have not occurred.

Ten patients, whose cases are reported below, were treated at the Connaught Hospital (Army Chest Centre) during a period of four years. The first two cases have been briefly reported previously (Davies, 1957).

Case 1

A signalman aged 19 was referred for investigation of malaise, productive cough, and right-sided pleuritic pain of four weeks' duration. Fifteen months earlier he had been treated for a right-lower-lobe pneumonia. During this illness there was radiological evidence of a large thin-walled lung cavity, which disappeared after treatment with antibiotics and postural drainage. On discharge from hospital his chest *x*-ray film had been reported to show no residual abnormality. After this illness he had continued to have a slight productive cough but had felt fit and led an active life.

The only abnormal physical findings on admission were diminution of breath sounds and a few rhonchi at the right base.

Investigations.—Postero-anterior (P.A.) and lateral chest radiographs showed a cyst 8 cm. in diameter, with a fluid level, situated in the posterior basal region of the right lower lobe. Lateral tomograms showed a multicystic mass with several fluid levels. A bronchogram showed a small communication between the largest cyst and the posterior basal segmental bronchus. Screening gave no further information. The sputum contained only normal respiratory flora, and cultures for *Mycobacterium tuberculosis* were negative. The Mantoux test was negative (1/100 O.T.); both the E.S.R. and blood count were normal.

At operation (right lower lobectomy) a large cystic mass was found in the postero-lateral part of the right lower lobe. The mass was supplied by a large thin-walled artery which came up through the diaphragm alongside the aorta to enter the lung in the inferior pulmonary ligament. The cysts contained gelatinous material, and the presence of a small communication with the normal bronchial tree was confirmed.

Case 2

A major aged 45 was admitted to hospital having suddenly coughed up about half a pint (280 ml.) of blood. He said he had a "smoker's cough" and had been producing about a teaspoonful of purulent sputum daily for the past four years. He had no other symptoms, and, apart from some crepitations audible at the left base, there were no other abnormal findings on examination.

Investigations.—The P.A. chest radiograph showed a cystic opacity in the left lower zone partially obscured by the heart shadow. The lateral radiograph showed the opacity to be located in the posterior part of the lower lobe. Tomography showed a cyst about 1 in. (2.5 cm.) in diameter. Screening gave no additional information. Bronchography showed a normal bronchial tree, but a small amount of dye reached the cyst through a minute communication with a subsegmental bronchus. A second bronchogram a few weeks later failed to show the communication. Bronchoscopy was normal. The sputum contained only normal respiratory flora, and cultures for *M. tuberculosis* were negative. The E.S.R. and blood count were normal.

At operation (resection of basal segments of left lower lobe) an ill-defined cystic mass was palpable in the posterior part of the lower lobe. The mass was supplied by a large artery arising from the aorta just above the diaphragm. Several cysts were present in the specimen, but no communication between them and the bronchial tree could be found.

Case 3

A guardsman aged 22 had a short influenza-like illness, after which he developed a cough producing small amounts of mucoid sputum, and a low-grade fever which persisted despite a course of penicillin. A chest radiograph showed an opacity in the right lower zone, and he was referred to the Connaught Hospital for investigation. There was no history of previous chest illness, and a mass miniature radiograph three years earlier had been passed as normal. On admission he did not look ill, and there were no abnormal physical findings.

Investigations.—The P.A. chest radiograph showed a group of five or six spaces, with fluid levels, and each about 1 in. (2.5 cm.) in diameter, lying medially in the right lower zone. The lateral film showed this polycystic mass to be situated posteriorly in the right lower lobe. Tomography and screening gave no further information. Bronchography showed a normal bronchial tree with no evidence of communication with the cysts. The sputum contained only normal respiratory flora, and cultures for *M. tuberculosis* were negative. The Mantoux test was positive (1/100 O.T.); the E.S.R. was 75 mm. in one hour (Westergren) but the blood count was normal. The diagnosis remained in doubt and the patient was treated conservatively, with antibiotics and postural drainage, for three months prior to operation.

During this time there was considerable change in the radiological appearances, which suggested the diagnosis. At first the cystic spaces became less apparent and the whole opacity appeared more dense. Later one large cyst, 8 cm. in diameter and containing a fluid level, appeared; subsequently the fluid level disappeared but the "hair-line" cyst wall remained just discernible. During this time the patient appeared fit, but intermittent blood-streaking of his sputum occurred.

At operation (right lower lobectomy) a large cystic mass was found in the position of the posterior and lateral basal

segments of the right lower lobe. This was supplied by several small arteries which came through the diaphragm from the abdominal aorta.

The cysts contained clear gelatinous material, and no communication with the bronchial tree could be demonstrated.

Case 4

An officer cadet aged 24 was treated for a left lower lobe pneumonia. Sputum cultures at that time produced a profuse growth of pneumococci. There was a good initial response to penicillin, but after one week his fever returned, he had several haemoptyses, and a chest radiograph showed a cavity to be present. He was then given chlortetracycline, to which there was a good clinical response. On discharge from hospital he felt fit, and his chest radiographs showed only a small residual shadow in the posterior part of the left lower lobe. At a routine out-patient follow-up six weeks later a chest radiograph showed a cavitated opacity, and the patient was referred to the Connaught Hospital for investigation.

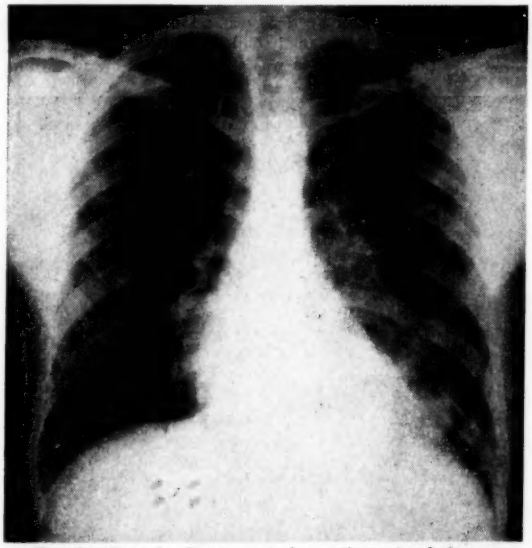

FIG. 1.—Case 4. Postero-anterior radiograph of chest.

FIG. 2.—Case 4. Lateral tomograph.

On admission he did not look well but was symptom-free, and there were no significant abnormal signs. There was no history of previous chest illness, and three routine mass miniature radiographs taken in the previous four years had been reported to be normal. As a child he had been in hospital for 10 months with suspected tuberculosis of the hip.

Investigations.—Chest radiographs showed an opacity, containing a thin-walled cyst 2 in. (5 cm.) in diameter, with a fluid level, apparently located in the posterior basal segment of the left lower lobe (Figs. 1 and 2). Tomography confirmed the presence of the cavity and surrounding opacity but gave no further information. Screening was normal, and bronchography showed a normal bronchial tree with no evidence of communication with the cavity. The sputum contained normal respiratory flora only. The E.S.R. and white-cell count were normal, and the Mantoux test was positive (1/1,000 O.T.). Bronchoscopy revealed no abnormality.

A provisional diagnosis of bronchopulmonary sequestration was made and thoracotomy arranged, but a few days before this was due to be performed sputum smears contained many acid-fast bacilli on three consecutive days. This coincided with the onset of cough and the disappearance of the fluid level.

On this account treatment with streptomycin and isoniazid was instituted and continued for three months. Serial chest radiographs showed the intermittent presence of fluid in the cavity and diminution of the surrounding opacity. No subsequent specimens of sputum contained acid-fast bacilli, and all cultures proved negative for *M. tuberculosis.*

At operation (left lower lobectomy) a cystic mass was present in the posterior basal region of the left lower lobe and was supplied by two large arteries which arose from the thoracic aorta just above the diaphragm. The mass contained two cysts, one filled with air and the other with gelatinous material; between the cysts there was a "honeycombed" area. There was no evidence of communication with the bronchial tree and no histological evidence of tuberculosis, and specimen cultures and guinea-pig inoculation were also negative.

Case 5

A major aged 37 was perfectly well until March, 1957, when he developed a productive cough and experienced several small haemoptyses. He was treated with penicillin and postural drainage, and soon became symptom-free. He was referred for further investigation as his chest radiographs showed a persisting opacity in the right lower lobe. There were no abnormal physical signs. He had a history of pneumonia at 3 years and of being "chesty" until 7; otherwise he had always been fit and athletic. Routine chest radiographs in 1953 and 1954 had been passed as normal.

Investigations.—The P.A. chest radiograph showed a rounded mass projecting beyond the right border of the cardiac shadow into the right lower zone. Lateral radiographs and tomograms showed a rounded mass about 6 cm. in diameter, with a small fluid level, in the postero-medial part of the right lower lobe. Screening and barium swallow gave no further information. Bronchography showed a normal bronchial tree with no evidence of communication with the lesion. Bronchoscopy was normal. The sputum contained only normal respiratory flora, and cultures for *M. tuberculosis* were negative. The E.S.R. and white-cell count were normal and the Mantoux test was positive (1/10,000 O.T.).

At operation (right lower lobectomy) a cystic mass was present in the postero-medial part of the right lower lobe; this was supplied by a large artery which passed up through the diaphragm. There were also several small arteries which came from the thoracic aorta. The cyst contained purulent material, and no communication with the bronchial tree could be demonstrated.

Case 6

A signalman aged 19 gave a history of three attacks of pneumonia affecting the right lung in childhood. An empyema occurred on one occasion, and was treated by rib resection and drainage. Subsequently he was fit and symptom-free for 10 years. Two months prior to his admission he had an influenza-like illness which had been complicated by a productive cough and one small haemoptysis. The cough persisted, and he continued to produced small amounts of sputum.

There were no abnormal physical signs beyond the scar from the rib resection in childhood and some limitation of movement at the right base.

Investigations.—The P.A. chest radiograph showed a rounded opacity about 1 in. (2.5 cm.) in diameter, with a fluid level, in the right lower zone. Tomography demonstrated a cystic mass situated postero-medially in the right lower lobe. Screening gave no further information. A bronchogram showed a normal bronchial tree with no evidence of communication with the cyst. The sputum contained only normal respiratory flora, and cultures for *M. tuberculosis* were negative. The E.S.R. and white-cell count were normal.

At operation (right lower lobectomy) a cystic mass was found in the postero-medial part of the right lower lobe which was supplied by an artery arising from the aorta just above the diaphragm. The cyst contained mucoid material. A small communication between it and the normal bronchial tree was present.

Case 7

A lance-corporal aged 38 had no chest symptoms until he developed an intermittently productive cough after an influenza-like illness. There were no abnormal physical findings. His only previous illness was due to a duodenal ulcer, for which a partial gastrectomy was performed in 1954—that is, four years earlier; his chest radiograph at that time was reported to be normal.

Investigations.—The P.A. chest radiograph showed an oval (2.5 by 5 cm.) cystic lesion in the right lower zone adjacent to the mediastinal shadow (Fig. 3). Tomography showed multiple cystic spaces apparently in the posterior basal segment of the right lower lobe (Fig. 4). Screening gave no further information. Bronchography revealed a communication between the posterior basal segmental bronchus and the cysts. Sputum cultures produced only normal respiratory flora; the E.S.R. was 30 mm. in one hour (Westergren); the blood count was normal and the Heaf test positive (grade III).

At operation (right lower lobectomy) a cystic mass about 5 cm. in diameter was found in the posterior basal region of the right lower lobe. Several small systemic arteries reached the mass via the inferior pulmonary ligament. It was not possible to demonstrate a communication between the mass and the bronchial tree.

Case 8

A trooper aged 36 was admitted to hospital complaining of right-sided pleuritic pain, a productive cough, and several small haemoptyses. He stated that for six years he had experienced recurrent episodes of productive cough and haemoptyses, although he had never produced large amounts of sputum or felt ill. There were no abnormal physical findings.

Investigations.—The P.A. chest radiograph showed an opacity, which contained an air space and a small fluid level, in the right cardiophrenic angle. The lateral film showed the opacity to be confined to the posterior part of the right lower lobe. Tomography and screening gave no further information. A bronchogram showed a normal bronchial tree with no evidence of communication with the cystic area. Sputum cultures produced only normal respiratory flora. The Heaf test was positive (grade II); the E.S.R. was 60 mm. in one hour (Westergren), but the white-cell count was normal.

At operation (resection of basal segments of the right lower lobe) a cystic mass was found in the postero-medial part of the right lower lobe, and this was supplied by a small artery arising from the aorta. No communication between the bronchial tree and the cyst could be found.

Case 9

A lance-bombardier aged 20 was admitted to hospital for investigation of an abnormal shadow seen on a routine mass miniature radiograph. He was symptom-free on admission,

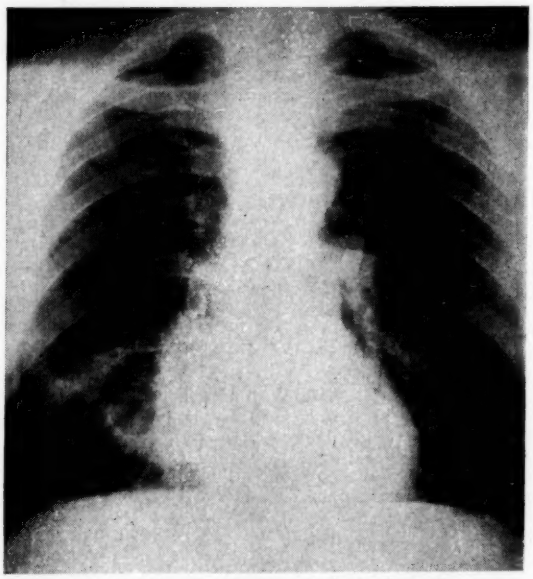

FIG. 3.—Case 7. Postero-anterior radiograph.

FIG. 4.—Case 7. Lateral tomograph.

but three months earlier had experienced right-sided pleuritic pain which lasted for five days. At the age of 10 he had been investigated for suspected pulmonary tuberculosis with reported negative findings; no details of this episode were available. There were no abnormal physical findings.

Investigations.—Chest radiographs showed a rounded shadow about 4 cm. in diameter in the right lower lobe. Tomograms showed this to be located in the region of the medial basal segment. Bronchography showed a normal bronchial tree; the lower lobe bronchi on the right side were displaced laterally by the mass. Sputum cultures produced only normal respiratory flora; the E.S.R. and blood count were normal and the Heaf test was negative.

At operation (resection of the basal segments of the right lower lobe) a mass 3.5 cm. in diameter was found in the medial part of the right lower lobe. This was supplied by an artery arising from the lower thoracic aorta. The mass felt firm and contained no cystic spaces on macroscopic examination. Histological examination showed the mass to consist of an outer wall of fibrous tissue and smooth muscle enclosing bronchioles lined by ciliated columnar epithelium and alveoli lined with cuboidal epithelium.

Case 10

This patient, a private aged 20, had no symptoms and there was no history of previous chest illness. An opacity had been noticed in the right lower zone on a routine mass miniature radiograph, and he was referred to the Connaught Hospital for further investigation. There was a congenital deformity of the thorax but no other abnormal signs.

Investigations.—Chest radiographs showed a cystic opacity about 4 cm. in diameter lying posteriorly in the right lower lobe. Tomography and screening gave no further information. Bronchography outlined a normal bronchial tree and failed to show any communication with the cystic mass. Sputum cultures produced only normal respiratory flora; the Heaf test was positive (grade III); the Casoni test was negative; and the E.S.R. and blood count were normal.

Thoracotomy was advised, but the patient refused this. He has since defaulted from the local chest clinic, but is known to have remained well for six months after discharge from hospital.

The radiological and bronchographic findings, normal E.S.R. and white blood count, with the absence of chest symptoms at any time, are considered to justify the presumptive diagnosis of bronchopulmonary sequestration.

Discussion

It is generally accepted that bronchopulmonary sequestration is congenital in origin, but there is no agreement concerning the mode of development of the condition. Several hypotheses have been put forward, and most of these presume the vascular anomaly to be the cause of the bronchopulmonary abnormality. The main views are: (*a*) that traction on the embryonic lung bud by the abnormal artery gives rise to the sequestration (Pryce, 1946); and (*b*) that insufficiency of the pulmonary artery supply to the developing lung bud results in persistence of vascular connexions between the primitive dorsal aorta and the developing lung (Jones, 1955; Smith, 1956). It has often been shown that branches of the pulmonary artery cannot be traced to the bronchopulmonary mass, which appears to be supplied by the aberrant artery alone.

It has been suggested that normal post-natal alveolar development fails because the affected lung tissue is perfused with oxygenated blood, and that the cystic changes occur after birth as a result of the systemic pressure of the blood supply (Smith, 1956).

More recently mechanical explanations of the pathogenesis of the defect have been questioned, and Boyden (1958) has expressed the view that there is no embryological evidence of a causal relationship between the arterial and bronchopulmonary anomalies. The variation in the combination of defects which can occur (Pryce, 1946), and the considerable variation in the size of the anomalous artery and its site of origin, are further factors which tend to suggest that the two components have an independent cause rather than that one causes the other. No satisfactory explanation for the liability of the sequestrated lung tissue to become infected has yet been given.

The clinical features described in this condition are variable; typically there is a history of recurrent pneumonia, pleurisy, or empyema (Pryce *et al.*, 1947); the symptoms commonly begin in the second decade (Pryce, 1946); and the lesion is said to be more common on the left than on the right side in the approximate ratio of 3:2 (Smith, 1955).

In the present series only one patient (Case 6) had what is said to be the typical history of recurrent pneumonia and empyema, although two others complained of a chronic cough of some years' duration. Two patients had experienced a previous chest illness—a pneumonia-like illness in Case 1 and pleurisy in Case 9. Of the remaining patients, four (Cases 3, 4, 5, and 7) had no history of previous chest symptoms and one (Case 10) had no symptoms at any time.

The ages of the patients at the time of their first symptoms attributable to the lesion ranged from 5 to 41 years. Several cases have been reported in which symptoms have dated from early infancy (Lalli *et al.*, 1954; McDowell *et al.*, 1955; Jones, 1955), and in others symptoms have not occurred until after the age of 50 years (Pryce *et al.*, 1947). In this series the lesion occurred more commonly on the right side (eight cases) than the left (two cases). Haemoptysis was a frequent symptom and occurred at some time in five of the patients.

Despite the gross radiological abnormalities, usually including cystic spaces with fluid levels, the illness resulting in admission was not severe in most of the patients, and they usually became symptom-free after treatment with antibiotics. The E.S.R. was often within normal limits, and leucocytosis was exceptional. These features are of some value in differentiating the condition from others which might give similar radiological appearances such as bronchiectasis, lung abscess, staphylococcal pneumonia, and tuberculosis.

Postero-anterior and lateral chest radiographs show a cystic or solid mass usually located in the postero-medial part of one or other lower lobe. The bulk and character of the opacities in serial radiographs tend to change frequently (McDowell *et al.*, 1955); this was evident in those cases observed for longer than a few weeks prior to operation.

In this connexion it is of interest that five of the patients had had previous routine chest radiographs which had been reported as normal.

By definition a sequestrated lung segment has no communication with the bronchial tree; when such a communication does exist with a lesion which satisfies the other criteria for description as a sequestrated segment, it is considered to have resulted from infection (Smith, 1955). These communications are small; their presence may be suggested by the finding of fluid levels

on the radiographs, which were seen at some stage in six of our cases. Sometimes bronchography will show the communication; this occurred in three of the patients, and in two of these fluid levels were not seen on the radiographs.

Despite careful dissection a communication was demonstrated in only two of the specimens. The poor correlation between the radiological and the pathological findings suggests that spontaneous closure of the communication occurs. This may be one reason for the considerable changes in the appearance of serial radiographs.

Tomography accurately demonstrates the situation and extent of the lung lesion but in our experience fails to outline the aberrant artery. This vessel may not be demonstrated even with the aid of angiocardiography (Pinney and Salyer, 1957). Anticipation of the presence of the vessel is essential in the event of surgical treatment, which might otherwise lead to catastrophic haemorrhage (Bruwer, 1955); but neither angiocardiography nor aortography appears warranted, since the likely presence of the artery should be inferred from the clinical and radiological characteristics of the condition.

Tuberculosis in association with bronchopulmonary sequestration has been reported on several occasions. The infection may involve another lobe of the lung (Tosatti and Gravel, 1951), the lung tissue adjacent to the defect (Edge *et al.*, 1957), or the sequestrated segment itself (Boyd, 1953; Smith, 1955; Johnston, 1956).

In one of our patients (Case 4) thoracotomy was undertaken with a provisional diagnosis of bronchopulmonary sequestration and associated tuberculosis, since acid-fast bacilli had been present in the sputum. Sputum cultures subsequently proved negative for *M. tuberculosis*, and no histological or bacteriological evidence of tuberculosis was found on examination of the resected specimen.

The natural history of bronchopulmonary sequestration is incompletely known. Most of the patients reported have been surgically treated and have had histories of repeated or chronic chest illness; there have been no follow-up reports of patients who have been treated conservatively. Since some patients have no symptoms until later life, intervals of many years between respiratory illnesses (10 years in Case 6) are not uncommon, and some patients become symptom-free after treatment with antibiotics, it is possible that the outlook without surgery is not always one of chronic respiratory ill-health. Resection offers a complete and permanent cure and is bound to commend itself when no general contraindication to surgery exists; nevertheless, there is some justification for regarding the recurrence of infection, rather than its occurrence, as the indication for surgery.

Summary

The clinical, radiological, and gross anatomical features of intralobar sequestration of the lung are described. Case reports of 10 patients are presented, nine of whom were operated upon. It is suggested that in patients with this condition a strong presumptive diagnosis may be made clinically.

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THE PREVALENCE OF ANAEMIA IN THE COMMUNITY

A SURVEY OF A RANDOM SAMPLE OF THE POPULATION

BY

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It is suspected that anaemia is common in Great Britain to-day, but, apart from some surveys of special groups of the community, no attempt has been made to determine its prevalence in the general population since the war.

In an attempt to obtain up-to-date information about the distribution of haemoglobin values, packed cell volumes, serum-iron and vitamin-B_{12} levels, and mean cell diameters, we have carried out surveys in population samples of two defined communities—one industrial and the other agricultural. We report in this paper the results of our first survey, which was done as a pilot study in a South Wales mining valley—the Rhondda Fach—in association with the Epidemiological Research Unit of the Medical Research Council Pneumoconiosis Research Unit (see Cochrane *et al.*, 1955), who had planned a survey of chronic bronchitis, ischaemic heart disease, and rheumatoid arthritis there during May and June, 1958.

Sample and Procedure

Details of the sample are shown in Table I. During the weeks between the census and the actual start of the survey 21 names had to be withdrawn (8 persons had died, 11 had left the area, and 2 had given erroneous date of birth), leaving an available sample of 779 subjects, of whom 193 were women and 586 men. These 779 subjects were visited and invited to come to a centre in Ferndale, the largest town of the Rhondda Fach. A total of 723 (543 men and 180 women), or 92.8% of this available sample, were examined. Between 30 and 40 people were seen each day and each person was in the centre for about 45 minutes, during which time many tests were made. In view of this fairly full

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programme it was impracticable to elicit symptoms which might have been attributable to anaemia, nor were we able to inquire into dietary habits. No attempt was made to diagnose anaemia on clinical grounds because of the known limited usefulness of inspection of the conjunctivae and hands (McAlpine *et al.*, 1957). We did not ask about the taking of iron tablets, but each person was directly questioned about injections which might have been given for Addisonian anaemia.

TABLE I.—*Random Sample*

Occupation Group	Age-group	Living in Valley at Census	Sampled	Proportion of Population	Died, Left Area, etc.	Refused	Examined
Miners and ex-miners	35–44	1,127	100	1/11	2	8	90
	45–54	1,283	100	1/13	—	5	95
	55–64	1,114	100	1/11	3	4	93
Non-miners	35–44	495	100	1/5	6	9	85
	45–54	338	100	1/3	3	8	89
	55–64	146	100	1/1·5	—	9	91
Women ..	55–64	1,535	200	1/8	7	13	180
Total ..		6,038	800		21	56	723

Methods

Venepuncture was done with iron-free 20-ml. all-glass syringes, using new needles (18 S.W.G.), and 2.5 ml. of blood was added to 25 mg. of dry E.D.T.A. (dipotassium salt) for determination of haemoglobin, packed cell volume, and preparation of blood films. The remainder of the specimen was placed in a sterile unused iron-free universal container for determination of serum-iron and serum-vitamin-B_{12} levels.

It was not possible to have a field laboratory in Ferndale, and the specimens taken during each day, most of them in the evening, were stored at 4° C. overnight in Cardiff. A pilot study in a small series of normal blood samples showed that storage in this way produced no significent change in haemoglobin level or P.C.V. During the next morning, haemoglobin and P.C.V. determinations were carried out, and two blood films made from each E.D.T.A. sample. The serum was separated from the clotted blood samples, using iron-free apparatus, and frozen at −20° C. until required for serum-iron and vitamin-B_{12} determinations.

Haemoglobin levels were determined in duplicate as oxyhaemoglobin in an E.E.L. photoelectric colorimeter, using a yellow-green filter (Ilford No. 625). P.C.V. were measured in duplicate after centrifuging in a Hawksley microhaematocrit for five minutes. Mean cell diameters (M.C.D.) were measured on thin unstained blood films by the diffraction method, using a Waterfield halometer. Leishman-stained blood films from each subject were examined. Serum-iron levels were measured by the method of Ramsay (1953) as modified by Jordan (1956). Serum-vitamin-B_{12} levels were determined by microbiological assay, using *Euglena gracilis* as described by Ross (1952). Both serum iron and serum vitamin B_{12} were estimated in duplicate whenever sufficient serum was available. Results of the M.C.D. and serum-vitamin-B_{12} estimations, together with their relationship to the other indices measured, will be published separately.

Before the survey began, arbitrary levels of haemoglobin, below which "anaemia" would be designated, were agreed upon—12.5 g./100 ml. (85%) or less in men and 12 g./100 ml. (81%) or less in women. If a subject was so designated, a red-cell count was done and the mean cell volume determined: a total and differential white-cell count and a reticulocyte count were also done. Each anaemic subject's general practitioner was immediately notified, and the patient was seen again, an offer of further investigation being made both to the patient and to the doctor.

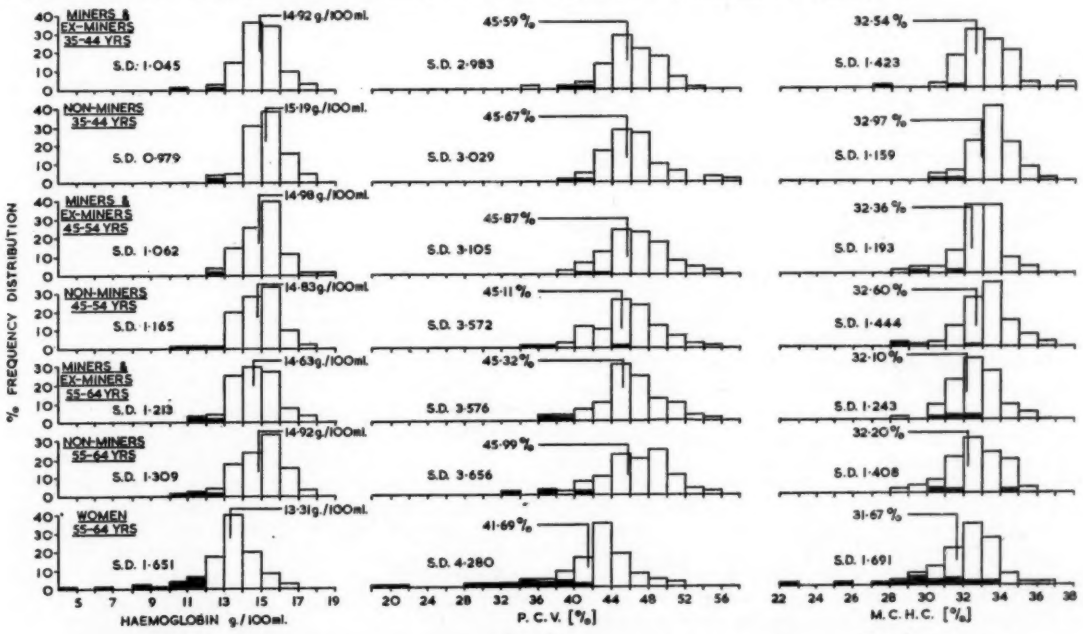

FIG. 1 FIG. 2 FIG. 3

FIG. 1.—Frequency distributions of haemoglobin values in a random sample of the Rhondda Fach. Black area = anaemia. FIG. 2.—Frequency distributions of P.C.V. values in a random sample of the Rhondda Fach. Black area = anaemia. FIG. 3.—Frequency distributions of M.C.H.C. values in a random sample of the Rhondda Fach. Black area = anaemia.

Results

Frequency Distribution of Haemoglobin Values.—The frequency distribution of haemoglobin values and the mean haemoglobin values for each group and their standard deviations are shown in Fig. 1. It can be seen that in respect of the mean values the group of women differ, as would be expected, from the rest. It can also be seen, however, that they have a larger spread of values and the distribution is skew, with a longer tail of lower values; the index of this is significant (g. = -1.767 ± 0.181). On analysis of the six groups of males the standard deviations are quite similar but the means differ significantly ($0.05>P>0.01$), and this appears to be a matter of overall spread for the six means, since no single simple comparison—for example, miners and non-miners—reaches the 5% level of significance.

Frequency Distribution of P.C.V. Estimations.—The women again differ from the men in means and standard deviation, as shown in Fig. 2, but the groups of men do not differ among themselves.

M.C.H.C. Estimations.—When the M.C.H.C. values were studied (Fig. 3) it was again seen that the women differed from the men, but there is also a significant difference in the mean M.C.H.C. between the six groups of men ($P<0.001$). This appeared to be due to significant differences between miners and ex-miners on the one hand and non-miners on the other, and to a significant regression of M.C.H.C. on age. Thus it can be shown that miners' and ex-miners' M.C.H.C. $=33.46-0.023 \times$ age, while non-miners' M.C.H.C. $=34.55-0.039 \times$ age. The two slopes -0.023 and -0.039 do not differ significantly ($t=1.262$; $0.30>P>0.20$) and Fig. 4 shows these slopes fitted to the data. The difference in level of M.C.H.C. at all ages is significant ($t=2.128$; $0.05>P>0.02$). Thus it may be concluded from our findings that at all ages miners and ex-miners have a lower M.C.H.C. than non-miners, and that the M.C.H.C. declines with age at an average rate of 0.031% per year. It appears that in non-miners M.C.H.C. falls faster and in miners and ex-miners more slowly than the average, but this difference may be a chance one.

Serum Iron.—Of the 723 subjects examined, sufficient serum was available in all but six of the men and three of the women, giving a total of 714 specimens. The mean serum-iron concentration of the miners and ex-miners, taking all age-groups together, was 118.4 μg./100 ml., and of the non-miners 123.3 μg./100 ml. Thus there is a statistically significant difference between these two occupational groups of 4.9 ± 1.08 μg./100 ml., though it seems unlikely that this difference is of any clinical significance. It can be shown that there is a positive correlation, though of low degree, between serum iron and M.C.H.C. (+0.19), but that there is little or no correlation between serum iron and age over the groups studied. Of the women studied the mean value for serum iron was found to be much lower than that of the men—namely, 103.8 μg./100 ml. These mean figures agree with those usually accepted for normal men and women.

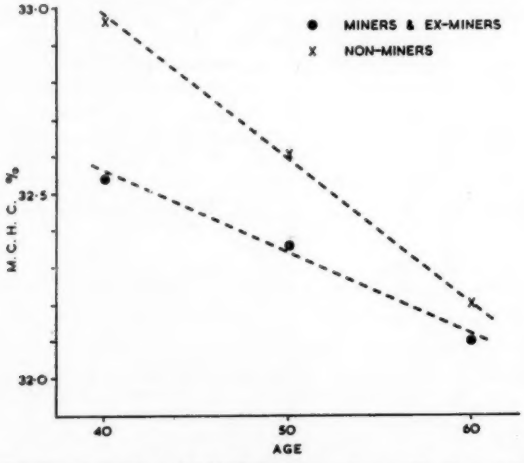

FIG. 4.—Comparison of M.C.H.C. of non-miners with miners and ex-miners in a random sample of Rhondda Fach men.

Cases of Anaemia

The prevalence of anaemia in the various age-groups is given in summary in Table II. The histograms (Figs. 1, 2, and 3) show the way in which the cases of anaemia are distributed throughout a considerable range of P.C.V. and M.C.H.C. values. An attempt was made to find the cause of the anaemias, but there was a disappointing response to our offer of further investigation in hospital. We decided, therefore, to discover what we could by questioning the anaemic people in their homes.

Anaemia in Men.—Table III shows details of the 18 cases of anaemia and gives the known or probable aetiological factors. Because of the small numbers in each group no breakdown for age or occupation has been made. Three men included in the sample were receiving vitamin-B_{12} treatment for Addisonian anaemia; none of these was anaemic.

TABLE II.—*Prevalence of Anaemia in the Various Groups of Subjects Examined. Anaemia Designated if Haemoglobin 12.5 g./100 ml. (85%) or Below in Men, 12 g./100 ml. (81%) or Below in Women*

Subjects	Age	Cases of Anaemia	
		No.	Percentage
Miners and ex-miners ..	35–44	2	2·2
Non-miners	35–44	2	2·4
Miners and ex-miners ..	45–54	2	2·1
Non-miners	45–54	3	3·4
Miners and ex-miners ..	55–64	5	5·4
Non-miners	55–64	4	4·4
Total		18	3·3
Women	55–64	25	13·9

TABLE III.—*Details of 18 Cases of Anaemia in Men*

Type of Anaemia	Hb (g./100 ml.)	Age	Probable Aetiological Factors
Hypochromic M.C.H.C.<31% (8 cases)	10·5	43	Deficient diet (mentally defective)
	10·6	47	Peptic ulcer
	11·1	58	Partial gastrectomy
	11·6	55	No obvious cause
	12·2	44	Peptic ulcer
	12·4	51	Partial gastrectomy
	12·4	46	Chronic lymphatic leukaemia
	12·5	64	Recent prostatectomy with blood loss
Borderline hypochromic M.C.H.C. 31% (6 cases)	11·4	64	Deficient diet (living alone)
	11·5	59	Carcinoma of stomach
	11·6	59	,, ,, larynx
	12·1	42	Peptic ulcer
	12·4	38	No obvious cause
	12·5	46	Partial gastrectomy
Orthochromic M.C.H.C.>31% (4 cases)	10·8	59	Chronic renal disease
	11·1	52	? malabsorption syndrome
	12·0	61	Haemorrhoids
	12·2	56	No obvious cause

Anaemia in Women.—Table IV summarizes the cause of anaemia adjudged to be the most important in each case, and iron-deficiency hypochromic anaemia is clearly shown to be the most common type found.

TABLE IV.—*Details of 25 Cases of Anaemia in Women*

Type of Anaemia	Hb (g./100 ml.)	Age	Probable Aetiological Factors
Hypochromic M.C.H.C.<31% (17 cases)	4·1	62	Deficient diet; no other obvious cause
	8·2	61	No obvious cause
	8·2	58	Deficient diet
	8·9	58	" "
	9·7	64	" "
	9·8	63	Deficient diet and haemorrhoids
	10·0	60	Deficient diet
	10·2	56	Previous heavy menstruation
	10·7	59	" " and deficient diet "
	10·8	58	No obvious cause
	11·2	64	Deficient diet
	11·2	61	" "
	11·4	56	Previous heavy menstruation
	11·5	57	Deficient diet and haemorrhoids
	11·5	63	Previous heavy menstruation and deficient diet
	11·6	60	Previous heavy menstruation
	11·8	60	No obvious cause
Borderline hypochromic M.C.H.C. 31% (5 cases)	10·3	56	Haemorrhoids
	10·4	56	Previous heavy menstruation
	10·7	58	Haemorrhoids
	11·1	61	Previous heavy menstruation
	11·4	63	Haemorrhoids
Orthochromic M.C.H.C.>31% (2 cases)	11·7	57	Fibroids
	11·9	61	Previous heavy menstruation
Macrocytic (1 case)	6·8	62	Addisonian anaemia (serum vitamin B_{12}, 27 $\mu\mu$g./ml.)

Follow-up Study on the Anaemic Subjects

While the main purpose of any epidemiological study is to inaugurate preventive measures, actual cases of disease discovered during a survey require further investigation and treatment. As most of the cases of anaemia discovered were of the hypochromic type we decided for reasons of practicability to offer iron to all the anaemic subjects. The patients' general practitioners were asked to prescribe oral ferrous sulphate 3 gr. (0.2 g.) t.d.s. for six months. At the end of this time the 43 subjects originally found to be anaemic were visited at home to get a further specimen of blood. Two of the 43 had left the area and two had died from disease known to have been present at the time of the initial survey—one from carcinoma of the stomach and one from advanced renal disease. Of the remaining 39, 24 were women and 15 men.

Men.—In the follow-up examination of the 15 men the haemoglobin had risen in 13 and fallen in 2, but 4 were still anaemic. Table V shows that, whereas there

TABLE V.—*Follow-up Results in 15 Anaemic Men*

	Initial Survey	Follow-up
Mean haemoglobin (g./100 ml.)	11·8	13·2
" M.C.H.C. (%)	30·1	30·8
" serum iron (μg./100 ml.)	75·6	69·6

was an increase in the mean haemoglobin values, the mean M.C.H.C. had barely increased and the mean serum-iron level had fallen slightly.

Women.—Of the 24 women examined, the haemoglobin had risen in 20, remained the same in 1, and fallen in 3, but 8 were still anaemic. Of the 16 subjects with iron deficiency studied, only 12 showed a rise in haemoglobin, but it may well be that the iron prescribed was not taken regularly. Table VI shows the increase in

TABLE VI.—*Follow-up Results of 24 Anaemic Women*

	Initial Survey	Follow-up
Mean haemoglobin (g./100 ml.)	10·2	12·7
" M.C.H.C. (%)	29·3	31·0
" serum iron (μg./100 ml.)	59·4	81·8

mean haemoglobin, M.C.H.C., and serum-iron values after the iron therapy. The one subject with Addisonian anaemia showed an excellent response to vitamin-B_{12} therapy.

Discussion

Because of inevitable differences in techniques employed in previous haematological surveys it is difficult and probably unwise to compare our data too closely with other results. Furthermore, in some previous surveys the detailed age structure of the population studied has not been given, while in others only selected groups of the population have been examined—Service personnel (Shorthouse and King, 1951), certain groups of adults and children (Berry *et al.*, 1952), and the elderly (Hobson and Blackburn, 1953).

It may be said, however, that on the whole the mean haemoglobin levels of 14.9 g./100 ml. for the men (aged 35–64) and 13.3 g./100 ml. for the women (aged 55–64) in the Rhondda are lower than those found by Berry *et al.* (1952) and slightly lower than that of the M.R.C. survey (1945). Thus Berry *et al.* (1952) found a mean haemoglobin value of 15.9 g./100 ml. for male clerical workers and 15.6 g./100 ml. for male factory workers. They also found a mean haemoglobin value of approximately 14.1 g./100 ml. in employed women, and of 13.5 g./100 ml. in housewives. In the M.R.C. survey (1945) the results were 102.2% (Haldane) for men and 93.7% for women—all age-groups being included. That the men in our survey do not show higher mean values for haemoglobin is perhaps surprising because of the possibility of polycythaemia occurring in association with the chronic respiratory disease prevalent in the miners and ex-miners.

The P.C.V. values are much what one would expect, but the M.C.H.C.s are rather more interesting. On the whole the mean figures for M.C.H.C. in all groups studied were low—none was as high as 33%. The fall of M.C.H.C. with increasing age is an interesting finding, as is the fact that at all ages the values for miners and ex-miners are lower than for non-miners. The values for serum iron are also lower in the miners and ex-miners than in the non-miners, but there is no evidence that they fall with increasing age, at least over the age-groups studied in this survey. Thus it may be inferred that, whatever is responsible for the fall in M.C.H.C. with age, it is independent of the correlation of M.C.H.C. and serum-iron level. The most likely explanation of these findings is that increasing age results in a slight diminution of iron utilization for haemoglobin synthesis without affecting the total iron economy of the body. The occupational difference may possibly be explained by some genetic factor, but more probably by some difference in working conditions, financial status, or dietary habits, details of which have not been investigated.

The serum-iron concentrations in all our subjects were estimated in an attempt to obtain some measure, other than the M.C.H.C., of iron deficiency in the general population. A community survey of serum-iron levels has not been done before, and we therefore have no figures with which to compare them. Whether the serum-iron level is in fact a satisfactory index of iron deficiency is open to some doubt because it is subject to fluctuations at different times of the day, from one day to the next, and in association with infections (Ramsay, 1957). It may therefore be that the measurement of serum iron is not a very rewarding investigation

in epidemiological studies, as it is tedious and time-consuming, and requires much special preparation of glassware. It is hoped that more detailed information will be available later, when a comparison with our rural community is made. It is possible that measurement of the total iron-binding capacity of the serum might have been of more value than the serum iron, but shortage of serum and time precluded this.

As we did not know the frequency distribution of haemoglobin values in this part of the country before our survey started, we decided on arbitrary figures below which anaemia was to be designated—12.5 g./100 ml. (85%) or less in men and 12 g./100 ml. (81%) or less in women. These figures are similar to those used by Davidson *et al.* (1943), who designated "clinical anaemia" as being present in men when the haemoglobin was less than 85% (Haldane) and less than 80% in women. From a review of our frequency distributions of haemoglobin values it would appear that the arbitrary level chosen for women is a reasonable one but that the figure for men may be too low. It is difficult to be dogmatic about this, for while we have now examined a random sample of the general population we cannot claim that our subjects were necessarily normal. For this reason no simple statistical concept of normality can be evoked such as, for example, designating as normal those values which do not differ from the mean by more than twice the standard deviation of the mean value. It is of interest to note than in a W.H.O. (1959) publication dealing with the detection and evaluation of the anaemia problem of a community it is recommended that anaemia be considered to exist when the haemoglobin value is less than 14 g./100 ml. in men and less than 12 g./100 ml. in women.

We would have liked to know more about the cause of the anaemia discovered, but this proved difficult in practice. As a general therapeutic measure, however, it was decided to offer iron to all our anaemic subjects and to keep them under observation for six months. As workers in this and other fields have found, however, not all subjects so enjoined take prescribed medication regularly: some of our subjects failed to return to their doctors for a further supply of iron; some doctors failed to prescribe further iron; some subjects attributed dyspepsia, some constipation, and a few diarrhoea to iron therapy.

Iron-deficiency anaemia was the commonest type found, and it is suggested that the rather high prevalence of post-menopausal iron-deficiency anaemia in women is due to a chronic anaemia starting during the child-bearing years, followed by a diet inadequate in iron-containing food, protein, and ascorbic acid. In the men in this series the anaemia discovered has been of more sinister import than in the women. In both sexes a number of subjects who had been designated as having borderline hypochromic or normochromic anaemia responded satisfactorily to the administration of iron, thus supporting Beutler's (1959) contention that a degree of iron deficiency may exist in some people without hypochromia.

It is usually held that present or past blood loss is the most important factor in the pathogenesis of iron-deficiency anaemia, and this has been stressed again in this country by Bedford and Wollner (1958) in their study of elderly hospital patients, although "idiopathic" hypochromic anaemia has been described in Service personnel (Shorthouse and King, 1951; Leonard, 1954; Forshaw, 1954). We do not know how much intestinal blood loss has contributed to the anaemia discovered in either the men or the women in this series. In order to discover this it would have been necessary to test faeces for occult blood or to look for haemorrhoids, but it is very doubtful if either a stool collection or a rectal examination of a random sample of the community would have been viewed with favour or equanimity by the people on whose co-operation the success of such studies as this depends.

Summary

A survey to determine the prevalence of anaemia has been carried out in over 90% of a random sample of 600 men (300 miners and ex-miners, 300 non-miners) between the ages of 35 and 64, and of 200 post-menopausal women aged 55 to 64 living in an industrial community in South Wales.

The mean haemoglobin level for men was 14.9 g./100 ml. and for women 13.3 g./100 ml. In the men, the miners and ex-miners have been shown to have both a lower M.C.H.C. and a lower serum-iron concentration than the non-miners. There is a progressive fall of M.C.H.C. in both groups with increasing age.

Three per cent. of men had haemoglobin levels to 12.5 g./100 ml. or less, and 14% of women had haemoglobin levels of 12 g./100 ml. or less. The majority of these cases designated as anaemic were of the hypochromic type. Further investigation and therapy were offered to those discovered to be anaemic, and it was found that the women responded to iron therapy better than the men.

This survey could not have been carried out without the assistance and advice of many people. It is a pleasure to acknowledge our indebtedness in particular to Professor A. L. Cochrane and to the members of his epidemiological research team of the Medical Research Council Pneumoconiosis Research Unit; to the Board of Governors of the United Cardiff Hospitals for their help and ready provision of facilities to one of us (G.S.K.), who held a Cardiff Royal Infirmary Research Fellowship in Medicine during the time of this survey; to Mr. P. D. Oldham, of the Medical Research Council, for detailed statistical analysis and advice; to the staffs of the medical unit and institute of pathology of the Welsh National School of Medicine for very considerable secretarial and technical assistance; to Miss Sweet and Mr. R. J. Marshall, of the department of medical photography, who prepared the diagrams; to all the people of the Rhondda Fach who so willingly co-operated in this survey; and, finally, to Professor Harold Scarborough for his constant advice, interest, and encouragement.

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HAEMATOLOGICAL FINDINGS IN NON-WHITE SICK CHILDREN IN CAPETOWN

BY

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Previous investigations revealed the common occurrence of iron-deficiency anaemia in apparently healthy infants and pre-school children in the three main racial groups in Capetown (Lanzkowsky, 1959a, 1960, 1961). Treatment of these subjects with various oral iron preparations was followed by a significant rise in haemoglobin level (Lanzkowsky and McKenzie, 1959). Routine haemoglobin estimations of sick infants and children had revealed the frequent occurrence of low levels, and in view of the previous findings in healthy children it appeared important to determine haematological values in a series of these ill subjects.

Material

Haemoglobin estimations were done on 849 consecutive non-white infants and children attending the out-patient department of the Red Cross War Memorial Children's Hospital. Of these, 501 were Cape Coloureds and 348 were Africans.* Their ages ranged from 1 week to 6 years. As comparatively few white patients attend the hospital they were not included in this investigation.

Blood smears were examined and packed cell volumes (P.C.V.) and mean corpuscular haemoglobin concentration (M.C.H.C.) values determined in 100 of these patients, whose haemoglobin levels were found to be 0.5 g./100 ml. below the lowest figure accepted by Wintrobe (1956) as normal for each age-group.

The mean weekly family income was £4.12 in the case of Cape Coloured patients and £3.16 for African patients. These figures indicate that the Cape Coloured infants and children were from the "low-income" group and the Africans from the "medium-income" group in their respective sections of the community (Bronte-Stewart *et al.*, 1955; A. D. Moodie, 1959, personal communication).

In a sample of 332 of these out-patients 50.3% of Cape Coloured and 41.3% of African infants and children had been breast-fed for less than three months after birth. This is a much higher proportion than was found in healthy children in this community (Lanzkowsky, 1959a, 1960). In general all these patients had a poor dietary history.

The subjects for this study were taken seriatim from those attending the out-patient department for various ailments. Any patient who showed clinical signs of dehydration or who had a blood dyscrasia was excluded. They did not present primarily as cases of anaemia, and none had received iron other than that present in their usual diet. The majority of illnesses were acute and of not more than a few days' standing when the patient was brought to hospital. Table I details the diagnoses made in these infants and children.

*The Cape Coloured people are of mixed ethnic origin and the Africans consist of various tribes of indigenous groups of Southern Bantu. These people have a socio-economic status very much inferior to that of the white people.

Iron-deficiency anaemia in these cases was usually an incidental finding. Closer inquiry into the histories of these cases revealed four symptoms, present prior to the onset of the presenting illness, which could be attributed primarily to the presence of iron-deficiency anaemia. These were pallor, irritability, anorexia, and lassitude. Pallor of the mucosae was almost always present when the haemoglobin level was low. When the haemoglobin level was above 7 g./100 ml. the clinical assessment of anaemia on this criterion alone was often erroneous and could not be relied upon for the detection of anaemia. Anorexia, irritability, and decreased physical activity were found to be the commonest symptoms in those infants and children who were subsequently shown to have an iron-deficiency anaemia. In several patients, although the haemoglobin level was very low, there was no symptom which could be related to a deficit of iron.

TABLE I.—*Presenting Conditions of 849 Cape Coloured and African Infants and Pre-school Children Investigated*

Diagnosis	Cape Coloured	African	Total
No organic disease (behaviour disorders, crying at night, etc.)	37	30	67
Cardiovascular Disorders:			
Congenital heart disease	3	1	4
Rheumatic fever	1	0	1
Deficiency Diseases:			
Kwashiorkor	9	2	11
Marasmus	29	11	40
Rickets	7	16	23
Disorders of Eye, Ear, Nose, and Throat:			
Phlyctenular conjunctivitis	2	3	5
Otitis media	17	20	37
Tonsillitis	6	6	12
Gastro-Intestinal Disorders:			
Feeding problems	9	2	11
Gastroenteritis	159	127	286
Helminthiasis	15	6	21
Herpetic stomatitis	7	2	9
Infective hepatitis	1	0	1
Thrush	1	6	7
Infectious Diseases:			
Chicken-pox	2	3	5
Measles	5	7	12
Mumps	1	0	1
Whooping-cough	16	4	20
Neurological Disorders:			
Birth injury	1	0	1
Convulsions (febrile)	4	1	5
Mental deficiency	3	0	3
Respiratory Diseases:			
Bronchitis (with or without bronchospasm)	45	28	73
Bronchopneumonia	2	2	4
Coryza	58	33	91
Pneumonia	13	8	21
Tuberculosis	7	5	12
Skin Diseases:			
Allergic	9	14	23
Infection	25	10	35
Parasitic	7	1	8
Totals	501	348	849

Splenomegaly was occasionally found, but any associated systemic infection often causes splenomegaly in infants and children.

Methods.—Haemoglobin estimations were done on capillary blood by the oxyhaemoglobin method using a Klett-Summerson colorimeter previously calibrated against standard haemin and cyanmethaemoglobin solutions. P.C.V. determinations were made on venous blood by the standard Wintrobe (1929) procedure. Blood smears were stained by May–Grünwald–Giemsa method.

Results

The mean haemoglobin levels of sick Cape Coloured and African infants and pre-school children are shown in Table II. It reveals that the mean haemoglobin levels in the ill African infants and pre-school children in most age periods are higher than those groups in the Cape Coloured.

TABLE II.—*Comparison of Mean Haemoglobin Levels in Sick Cape Coloured and African Infants and Pre-school Children*

Age	Cape Coloured			African		
	No. of Cases	S.D.	Mean Hb (g./100 ml.)	Mean Hb (g./100 ml.)	S.D.	No. of Cases
Infants under 1 year of age						
1–1 month ..	17	3·06	14·44	14·25	—	2
1– ,, ..	28	2·44	11·42	11·35	3·93	13
2– months ..	28	1·23	9·88	10·57	0·95	17
3– ,, ..	45	1·22	9·99	10·37	1·40	31
4– ,, ..	35	1·43	10·19	10·54	1·45	30
5– ,, ..	33	1·51	9·97	10·38	1·02	12
6– ,, ..	33	1·61	10·27	9·94	1·04	16
7– ,, ..	36	1·75	10·05	9·97	1·47	27
8– ,, ..	25	1·55	9·79	9·96	1·63	16
9– ,, ..	27	2·11	9·43	9·74	1·27	11
10– ,, ..	22	2·13	9·47	9·34	2·03	24
11– ,, ..	28	1·67	9·14	9·82	1·88	14
Children 1 to 6 years of age						
1– year	49	1·98	8·81	9·47	1·83	46
2– years	29	1·58	9·37	9·42	2·09	25
3– ,, ...	11	1·44	9·99	11·01	1·44	21
4– ,, ...	15	1·23	10·71	10·82	1·00	18
5– ,, ...	20	1·96	10·66	11·00	0·84	12
6– ,, ...	20	1·31	10·73	11·39	1·24	13

TABLE III.—*Comparison of Mean Haemoglobin Levels in Cape Coloured and African Infants and Pre-school Children in Apparent Health and in Illness*

Age	Cape Coloured		African	
	Ill Hb (g./100 ml.)	Healthy Hb (g./100 ml.)	Ill Hb (g./100 ml.)	Healthy Hb (g./100 ml.)
Infants under 1 year of age				
First month ..	14·44	14·44	14·25	14·85
1 ,, ..	11·42	12·10	11·35	12·15
2 months ..	9·88	10·45	10·57	11·10
3– ,, ..	9·99	10·27	10·37	10·83
4– ,, ..	10·19	10·35	10·54	10·82
5– ,, ..	9·97	10·75	10·38	10·57
6– ,, ..	10·27	10·35	9·94	10·29
7– ,, ..	10·05	10·14	9·97	10·40
8– ,, ..	9·79	9·72	9·96	10·03
9– ,, ..	9·43	9·80	9·74	10·15
10– ,, ..	9·47	9·81	9·34	9·87
11– ,, ..	9·14	9·57	9·82	9·84
Children 1 to 6 years of age				
1– year	8·81	9·31	9·47	9·76
2– years	9·37	10·13	9·42	10·61
3– ,, ...	9·99	10·59	11·01	10·63
4– ,, ...	10·71	11·00	10·82	11·12
5– ,, ...	10·66	11·03	11·00	11·18
6– ,, ...	10·73	11·19	11·39	11·82

TABLE V.—*Mean Haemoglobin, P.C.V., and M.C.H.C. Values in 100 Sick Cape Coloured and African Infants and Children*

	Mean Value	Range	Standard Deviation
Hb (g./100 ml.)	8·35	2·3–10·9	1·76
P.C.V. (%)	31·35	8–45	6·56
M.C.H.C. (%)	26·30	17–31	2·79

Table III shows that the mean haemoglobin levels in the ill infants and pre-school children are lower than the values determined for apparently healthy infants and pre-school children (Lanzkowsky, 1959a, 1960, 1961).

Table IV shows the details of the 100 blood smears examined. The blood smears were assessed without knowledge of the exact haemoglobin value, and the Table shows the correlation between the iron-deficiency features of the smears and the corresponding haemoglobin levels. It will be seen that the lower the haemoglobin value the more likely was the smear to reveal the features of iron-deficiency anaemia.

The P.C.V. and M.C.H.C. values are shown in Table V. The low M.C.H.C. in each case confirmed the presence of iron-deficiency anaemia in every infant and child in this group.

Discussion

It was fairly clear in the early stages of this investigation that the mean haemoglobin levels of these non-white infants and children attending the out-patient department were much below the generally accepted normal levels for their age and below the mean haemoglobin levels for apparently healthy non-white infants and pre-school children.

A review of the literature failed to reveal any comparable investigation on infants and children in South Africa, and only a few surveys in other countries were found.

Guest *et al.* (1938) reported on 615 white infants and children, but in their analyses of haemoglobin levels they failed to distinguish between healthy and sick cases. For this reason, no conclusions relative to the present investigation can be drawn from their findings. Somerford (1938) found that 100 out of 179 debilitated children attending the out-patient department of the Royal Manchester Children's Hospital were anaemic. Her criteria for anaemia were a red-cell count of 4,000,000/c.mm. or less, and a haemoglobin level of under 70% on the Haldane scale. She made the surprising observation that children who were in better economic circumstances were more affected than those of poorer families.

Despite the fact that the mean haemoglobin levels of the infants and children in the present investigation were low and that the levels in some cases were very low, none of the 849 patients was brought to hospital primarily for symptoms which could be directly

TABLE IV.—*Details of Red Blood Cell Morphology and Correlation with Haemoglobin Ranges in 100 Sick Cape Coloured and African Infants and Children*

Hb Range (g./100 ml.)	No. of Cases	Normal R.B.C.s	Hypochromasia				Anisocytosis				Poikilocytosis			Polychromasia		Target Cells (Occasional)	Basophilic Stippling (Occasional)
			Sl.	+	++	+++	Sl.	+	++	+++	Sl.	+	++	Sl.	++		
2·0–2·9	1	—	—	—	—	1	—	1	—	—	—	1	—	1	—	—	—
3·0–3·9	1	—	—	—	—	1	—	—	1	—	—	1	1	—	—	1	—
4·0–4·9	5	—	—	1	3	1	2	2	—	1	1	2	—	2	—	—	—
5·0–5·9	2	—	—	—	1	1	—	1	1	—	—	—	1	—	—	—	—
6·0–6·9	6	1	—	1	2	1	1	2	—	1	—	2	—	2	1	—	1
7·0–7·9	24	—	4	6	9	3	6	9	4	1	1	2	1	3	—	3	—
8·0–8·9	17	—	6	5	4	—	9	2	—	1	—	1	—	2	—	1	2
9·0–9·9	36	12	16	3	3	—	7	2	—	—	3	1	—	—	—	—	1
10·0–10·9	6	3	1	2	—	—	1	—	—	—	—	—	—	—	—	—	—
11·0–11·9	2	1	1	—	—	—	—	—	—	—	—	—	—	—	—	1	—
Total	100	17	28	18	22	8	26	19	6	4	5	9	3	10	1	6	4
			76				55				17			11			

Sl. = slight.

attributed to the anaemia. On close questioning, most parents admitted that anorexia and decrease of physical activity had manifested, to a greater or less degree, before the onset of the illness which brought the children under observation. The mothers sought advice in most cases on account of infection. Of the 849 patients, 633 had infection. Histories of ascariasis were obtained in 21% of the Cape Coloured and 22% of the African patients.

The explanation of parental failure to seek medical attention for the anaemia almost certainly lies in the insidious nature of its onset and its slow progress. The absence of obvious signs and symptoms in these young children is attributable to the remarkable ability of the body to adjust itself to very low levels of haemoglobin. The physician often fails to recognize the condition, probably because his attention is focused on the presenting infection.

The symptoms of anaemia are usually recognized in retrospect by the parents after treatment has been instituted. Pallor, poor appetite, and decreased physical activity are often found in anaemic infants and children. Anorexia leads to the establishment of a vicious cycle in which the deficiency of iron is accentuated by a further reduction in dietary intake. Depraved appetite as seen in pica is less commonly reported, but it is of more significance than has been realized in the past (Lanzkowsky, 1959b).

In considering factors which may have contributed to the pathogenesis of the low haemoglobin levels which were found in infants and children in the present investigation, mention must be made of the influence of socio-economic status and the possible role of infection in these patients.

All the reports in the literature dealing with the question of the relationship between socio-economic status and haemoglobin level in healthy subjects conclude that low economic circumstances are associated with a lowered haemoglobin level (Fullerton, 1936; McCance *et al.*, 1938; Committee on Haemoglobin Surveys, 1945; Berry *et al.*, 1952). In the only report found on ill children, Somerford (1938) stated that the socio-economic status does not appear to influence the haemoglobin level. In the present series of ill infants and children the majority, who were Cape Coloured, came from the lowest-income group of their community. The correlation between socio-economic status and haemoglobin level was not investigated further.

Over the years many theories have been advanced on the pathogenesis of the anaemia associated with chronic infection. It appears most likely to be due to the result of impaired erythropoiesis and shortened survival of red blood corpuscles. Contributory influences may be: unusual affinity of reacting tissues for iron, direct blood loss into the inflamed area, and anorexia followed by inadequate intake of haemopoietic substances and impaired gastro-intestinal absorption of these substances during the illness (Wolman, 1957). In most instances infections of less than a month's duration are not accompanied by a significant anaemia (Wintrobe, 1956).

Lahey (1957) doubts whether infection *per se* in children causes anaemia but favours the view that it aggravates a pre-existing iron-deficiency state. Even if this limitation is accepted, repeated infections must have a cumulative effect which will sooner or later be significant. It is common knowledge that non-whites in Capetown are often infected in infancy. Iron-deficiency anaemia has been shown to occur in a high percentage of non-white infants and children. The facts revealed by the present work fit in very well with Lahey's concept. Furthermore, the custom, now apparently obsolete, of medical practitioners prescribing iron therapy routinely for the convalescent patients might well be revived to the advantage of such infants and children.

Summary

There have been no previous reports of investigations on haemoglobin levels in sick infants and pre-school children in South Africa and only very few publications of such studies in other countries.

Haemoglobin levels were determined on 849 non-white infants and children taken seriatim from those attending the out-patient department of the Red Cross War Memorial Children's Hospital. The mean haemoglobin values were found to be even lower than the mean values in apparently healthy infants and pre-school children in Capetown, among whom the occurrence of low haemoglobin levels has already been demonstrated. The mean levels in the Cape Coloureds were lower than in the Africans in almost all age groups. M.C.H.C. values determined in 100 cases in the series confirmed the presence of an iron-deficiency anaemia in every infant and child of this group.

The fact that none of the cases presented symptoms of anaemia despite the low haemoglobin levels emphasizes the insidious nature of onset and the slow progress of iron-deficiency anaemia in infants and children. After treatment parents appreciated that symptoms of anaemia had been present prior to treatment.

The roles of socio-economic status and infection in the aetiology and pathogenesis of iron-deficiency anaemia in these subjects are discussed.

I am indebted to Professor F. J. Ford, head of the department of child health, for his constant guidance and advice during the course of this work; to Dr. J. D. L. Hansen for his encouragement; to Dr. D. McKenzie for providing me with the facilities of his laboratory; and to Dr. J. F. W. Mostert, superintendent of the Red Cross War Memorial Children's Hospital, for permission to publish this work. Finally, I would like to express my gratitude to the matron and staff of the hospital for their willing co-operation, unfailing courtesy, and assistance rendered during the course of this investigation.

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URINARY TRACT INFECTION

A COMPARATIVE STUDY IN THE DIABETIC AND GENERAL POPULATIONS

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It is generally believed that diabetes mellitus predisposes to infections of the urinary tract and that these are commoner in the diabetic than in the general population. Most of the studies which confirm these opinions are based on the findings at necropsy on diabetics dying in hospital (Sharkey and Root, 1935; Baldwin and Root, 1940; Barnard *et al.*, 1953), in whom the incidence of terminal urinary-tract infection would be expected to be high. Studies on living diabetic patients often lack direct controls or fail to take age or sex into account. The relatively few, and contradictory, reports on the prevalence of infections of the urinary tract in the general population refer to patients in hospital (Ophüls, 1926; Loopuyt, 1946), or attending medical out-patient departments (Kass, 1956). However, Kass (1955) and others revived the use of quantitative bacterial counts obtained by culture of freshly voided urine, thereby providing a diagnostic method by which comparison between the diabetic and general population can be made. Such a study is here described.

Material and Methods

The age in 20-year groups and sex distribution of the current attenders at a large diabetic clinic (3,841 patients) was determined. 150 patients, whose age and sex correspond with that of the total clinic population, were selected at random and the freshly passed mid-stream specimen of urine was collected and cultured quantitatively by the methods described below. The identical procedure was carried out in 150 non-diabetic controls of similar age and sex distribution. These were patients attending the casualty department with minor trauma, and their friends and relatives. Care was taken to exclude any patient attending with other than minor trauma, since it was felt that in this way the controls would be as representative as possible of the general population.

Technique of Collection and Culture of Specimens.—In males the glans penis was swabbed with 1/1,000 benzalkonium chloride ("roccal") and a mid-stream specimen of urine collected. Female patients were prepared in the dorsal lithotomy position, as for catheterization, with the same antiseptic. The labia were separated, the patient was encouraged to void urine, and a specimen from the mid-portion of the urinary stream was collected into a sterile container. Specimens were dealt with immediately after collection. Serial tenfold dilutions of urine 1:10 to 1:1,000,000 were made in sterile normal saline, and 1 ml. of each dilution was mixed with 10 ml. of molten nutrient agar kept at 50° C., then poured into a Petri dish and allowed to set. The six plates were cultured aerobically at 37° C. for 48 hours. The plate containing approximately 50–200 colonies was counted, and the number multiplied by the dilution gave the number of viable organisms per ml.* Duplicates were at first put up anaerobically as well, but the total counts did not differ significantly, and this procedure was therefore discontinued.

A count of more than 100,000 organisms per ml. was considered to be indicative of infection of the urinary tract (see below). Counts below 10,000 per ml. probably represent the range of contamination, while counts of 10,000 to 100,000 per ml. are of doubtful significance (Kass, 1956; Merritt and Sanford, 1958).

Results

Table I shows the age and sex composition of both diabetics and controls. The preponderance of middle-aged and elderly women (determined by the large number of these in the diabetic population) is evident. Bacterial counts of more than 100,000 per ml. of urine were obtained in 20 (13.3%) of the diabetics and in 18 (12.0%) of the controls. Thus there was no significant difference in the incidence of infection of the urinary tract between the two groups.

TABLE I.—*Percentage Age and Sex Composition of 300 Subjects Studied*

Age:	0–19	20–39	40–59	60+
Females	2	6	17	36
Males	2	7	16	14

Table II shows the results of the bacterial counts for the 300 subjects and the striking similarity between diabetics and controls at every level of bacterial count can be seen.

Sex.—In Table II the sex incidence of the varying degrees of bacteriuria is also seen. The excess of females among those with infection of the urinary tract is striking: of the 20 infected diabetics 18 were women, while, of the controls, only one of the 18 subjects with infection of the urinary tract was male.

TABLE II.—*Bacterial Counts in 300 Subjects*

Organisms/ml. Urine		Females	Males	Total
More than 100,000	D	18	2	20
	C	17	1	18
10,000–100,000	D ..	11	6	17
	C ..	15	2	17
1,000–10,000	D ..	24	9	33
	C ..	24	10	34
0–1,000	D ..	19	29	48
	C ..	24	33	57
No count	D ..	19	13	32
	C ..	11	13	24

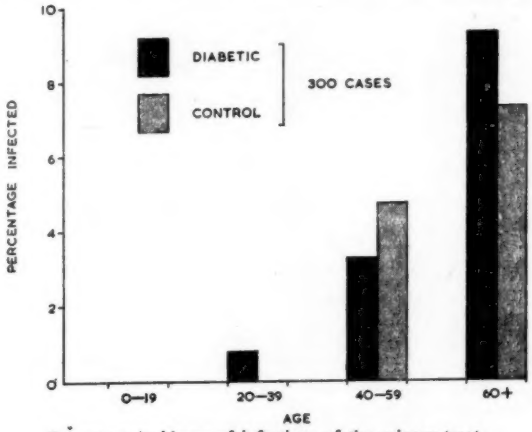
D=Diabetics. C=Controls.

Age.—The Chart shows the numbers infected in each 20-year age-group of both diabetics and controls, expressed as a percentage of the total numbers examined. In Table III the actual numbers of patients with infection of the urinary tract in the different age-groups are shown. In subjects up to the age of 40 we found only one infected urine in 25, but after this age the incidence of infection increased markedly, and, in the women aged 60 and over, 24 of 108 examined (22%) had bacterial counts of over 100,000 per ml.

*As an alternative, a standard-sized loopful of freshly voided urine can be rubbed over the surface of an agar plate. With a conversion graph, the colony count obtained by this method can be correlated with the viable count as obtained above. This latter method obviates the lengthy procedure required in the dilution technique (O'Sullivan *et al.*, 1960).

TABLE III.—*Age Distribution of the 38 Patients with Infection of the Urinary Tract*

Age:	0–19	20–39	40–59	60+
Diabetics	0	1	5	14
Controls	0	0	7	11
Totals ..	0	1	12	25



Percentage incidence of infections of the urinary tract.

Bacteriology

The identification of the bacterial species found in the urine in relation to the various colony counts is of interest and is shown in Table IV. In urines with high bacterial counts, coliform organisms were the commonest found and often in pure culture. The other common pathogens of the urinary tract, *Proteus vulgaris* and *Bacillus lactis aerogenes*, were also relatively frequent at higher counts. In the low count specimens *Staph. albus* and diphtheroids—the common contaminants—were the usual bacteria isolated in colony cultures, while *Escherichia coli* and *P. vulgaris* were relatively infrequent. These findings, also noted by others (Kass, 1955, 1956; Huvos and Rocha, 1959), increase the significance of high bacterial counts. It can be seen, too, that there was no significant difference in the bacterial flora of the diabetics and the controls.

TABLE IV.—*Organisms Found at Various Levels of Bacterial Counts*

	>100,000		10,000–100,000		1,000–10,000		0–1,000	
	D	C	D	C	D	C	D	C
E. coli	11	6	1	3	1	3	4	3
P. vulgaris ..	2	2	1	2	0	2	2	2
B. lactis aerogenes	1	1	1	1	2	0	1	2
Str. faecalis	1	4	5	2	10	3	3	3
Staph. albus and diphtheroids	5	5	9	9	20	26	37	47

D=Diabetics. C=Controls.

The one respect in which the diabetic patients differed from the controls was the height of the bacterial counts among those infected. Of the 20 diabetics considered to have infection of the urinary tract because of counts of more than 100,000 organisms per ml., 15 had counts of more than 1,000,000 per ml., while only 7 of the 18 infected controls had counts in this latter range. If the number of bacteria grown is an index of the severity of the infection, then, while the incidence of infection is the same in both groups, the diabetics seem to be more severely affected. A more probable explanation is that the infected diabetic patients had heavy glycosuria at the time the specimen was collected and the presence of glucose rendered the urine a more favourable medium for the multiplication of organisms. The influence of glycosuria on bacterial counts was investigated further, and it was found that the addition of 2% of glucose to normal urine inoculated with *E. coli in vitro* caused a fourfold increase in the bacterial count after two hours at 37° C.

Discussion

The wide discrepancy between the frequency of pyelonephritis in necropsy material, where it has been found in from 6 to 20% of cases, and its prevalence in living patients led several observers to seek methods of assessing infection of the urinary tract other than the traditional one of microscopy and qualitative culture of the catheter specimen of urine in the female and the mid-stream specimen in the male. The growing evidence implicating catheterization (Guze and Beeson, 1956; Beeson, 1958) as a factor in the pathogenesis of infection of the urinary tract has stressed further the desirability of a reliable method of evaluating non-catheter urine specimens. The revival of quantitative bacterial counts by serial dilution of urine specimens led to a new interest in this subject and to a number of publications concerning the prevalence of asymptomatic infections of the urinary tract in various groups of hospital populations.

The findings to date indicate that contamination and true bacteriuria may be distinguished by counting the numbers of bacteria in the urine (Kass, 1955). This has been confirmed by correlations between bladder urine aspirated through the abdominal wall and clean-catch mid-stream specimens (Monzon *et al.*, 1958) and between catheter specimens and clean-catch specimens (Boshell and Sanford, 1958; Merritt and Sanford, 1958). MacDonald *et al.* (1957), collecting bladder urine after death and correlating the colony counts with the pathological findings at necropsy, conclude that bacterial counts are a reliable means of detecting true bacteriuria and that such bacteriuria is often associated with active infection of the kidneys and other structures of the urinary tract. There is some difference of opinion about the initial level of bacterial count above which infection of the urinary tract is considered to be present, figures of from 10,000 to 100,000 being quoted by various workers (Kass, 1956; Huvos and Rocha, 1959), but all are agreed that counts above 100,000 per ml. are significant; therefore our results certainly do not overestimate the incidence of infection.

The main finding of the present investigation—that infection of the urinary tract is no more common among diabetics than among non-diabetic controls from the general population—is in disagreement with current opinions, which may be summed up by Beeson's (1955) statement, "urinary tract infection is commoner in diabetics than in non-diabetics, although precise data on this is lacking." It is claimed on hypothetical grounds that metabolic disturbances in diabetes influence directly mechanisms of resistance to infection. Yet in experimentally produced diabetes no significant alteration in resistance to administered pathogens has been observed (Perla and Marmorston, 1941; Schofield and Baker, 1956), while at necropsy Robbins and Tucker (1944) found that the incidence of infections other than renal ones was about the same in diabetic as in non-diabetic patients. Clinical impressions have always suggested an increased incidence of infection of the urinary tract

among diabetics, but since both diabetes and infections of the urinary tract occur most commonly in middle-aged and elderly women, it is not surprising that the number of diabetics with infections should seem large. The greater hazard of infections in diabetic patients serves also to make them more memorable.

Previous reports have, with one exception (Huvos and Rocha, 1959), found a higher incidence of infection in diabetics than in non-diabetics. The great majority, however, base their findings either on the results of necropsies on patients dying in hospital or on hospital in-patients. The lack of controlled studies on a diabetic out-patient population and "healthy" non-diabetics is surprising. Thus Barnard *et al.* (1953), in a series of 100 necropsies on diabetics dying in hospital, found that 30% had suffered significant infection of the urinary tract. Merritt and Sanford (1958) examined 100 consecutive ambulatory and non-ambulatory admissions to a medical ward and found a significant excess of patients with diabetes in the group with positive cultures. It is probably invalid to apply results from an investigation such as this, based on hospital admissions, to a general population, either diabetic or non-diabetic, particularly as Rengarts (1960), studying diabetic admissions to the Joslin Clinic Service, found a much higher incidence of urinary infections in patients confined to bed than among ambulatory diabetics. In this latter study the incidence of infection among ambulatory diabetics (14% of 43 patients) was very similar to the present findings.

That infections of the urinary tract are commoner in women than in men has long been recognized, and a marked excess of infected females is seen in the present series, as in others (Kass, 1955, 1956; Rengarts, 1960). The striking significance of age in determining the incidence of infection is not so widely appreciated, but where it has been taken into account the number of patients infected has risen steadily with age in both diabetics (Huvos and Rocha, 1959) and non-diabetics (Loopuyt, 1946). Kass, in an extensive study, found that 18% of 54 female diabetics and only 6% of 337 females attending as out-patients had infections of the urinary tract, but makes no mention of the ages of either group, so that it is difficult to assess the significance of his findings. Failure to take into account the large numbers of middle-aged and elderly women in the diabetic population is probably the main reason for the present confusion of thought on this subject.

Finally, although adequate figures are available regarding the incidence of infections of the urinary tract in hospital in-patients (Marple, 1941; Loopuyt, 1946), there is a striking lack of information about the general population. The need to obtain catheter specimens of urine from the female for reliable bacteriological and microscopical study has in the past been an understandable deterrent. Quantitative examination of clean-catch voided specimens now provide a safe and relatively simple method of evaluating infections of the urinary tract, and its use in "healthy" populations such as the controls in the present study could with advantage be extended further. Only in this way will the significance of asymptomatic infections be recognized, their possible association with other disorders such as hypertension be elucidated, and methods for their control be put on a more effective and adequate basis.

Summary

The use of quantitative bacterial counts on clean voided urine specimens is described.

A comparison of the incidence of infections of the urinary tract in 150 randomly selected diabetics, representative of a large diabetic clinic, with a similar number of non-diabetic "healthy" controls shows no significant difference between the two groups.

The high incidence of infection of the urinary tract in middle-aged and elderly women in both groups is noted and its significance discussed.

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VARICOCELE: A TREATABLE CAUSE OF SUBFERTILITY

BY

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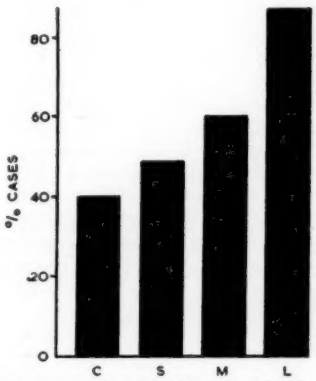
Disappointment at the results of drug therapy in the treatment of male subfertility (Scott, 1959) has given way to increasing optimism as regards the results now being achieved by surgery. Before Tulloch (1952) first reported restoration of fertility in an azoospermic man after varicocele ligation, a varicocele was seldom if ever considered as a possible cause of subfertility. Russell (1954) later noted that the incidence of varicocele was much greater in men attending a subfertility clinic than in the husbands of women attending his antenatal clinic. Finally, I showed that subfertility could be detected in 66% of varicocele patients compared with only 39% of those with no varicocele (Scott, 1958a). Persistence of a varicocele beyond the age of 30 years resulted in progressive deterioration of fertility in the cases studied by Russell (1957), and I subsequently reported three cases of progressive subfertility over a period of five years which was finally checked and returned to acceptable fertility by varicocele ligation (Scott, 1960a).

The incidence of subfertility appears to be in direct proportion to the size of the varicocele (see Chart). In a previous communication (Scott, 1958b) I showed that the effects on the sperm count and sperm motility were also related to the size of the varicocele. A later study (Scott, 1960b) confirmed this clinical impression by demonstrating that the greatest improvement followed operation on the largest varicoceles, ligation of small varicoceles gave the poorest results, and control ligation of the spermatic veins in subfertile volunteers with no varicocele produced no change in fertility at all.



Incidence of subfertility associated with different sizes of varicocele. C= Controls with no varicocele. L= Cases with large varicoceles. M= Moderate varicoceles. S=Small varicoceles.

Davidson (1954), Tulloch (1955), and Young (1956) have already, between them, reported 52 varicocele ligations, with seminal improvement in 77%. Unfortunately, many of their critics believe that these successes can be attributed to the normal fluctuation of sperm count and motility, as described by MacLeod and Gold (1956). In order to refute these criticisms and overcome the possibility of error in assessing the value of this operative procedure, the seminal findings have been "ranked" in this study, and only improvement to a higher rank was considered significant.

Material and Method

Of the 108 subfertile men whose varicoceles have been ligated in this clinic, 11 have since left the district and have not been traced, while four were operated on too recently to be included in this study. Pre- and post-operative seminal studies were carried out on 82 cases with pre-operative subfertility and on six cases of pre-operative azoospermia. Another five men have declined further seminal investigation but have notified a successful pregnancy since operation.

Varicocele ligation and division at the deep inguinal ring was performed on 108 men with left-sided varicoceles which, *with the patient standing upright*, were greater than the diameter of the index finger.

As it had previously been shown (Scott, 1958b) that the deleterious effects of varicocele were most pronounced on the sperm count and sperm motility, "subfertility" was taken to denote a sperm count below 20 million per ml. or a sperm motility showing less than 50% of the sperms actively progressive five hours after ejaculation. Two or more seminal samples were studied before and after operation, and the figures referred to in the text represent an average of these readings. Allowance for normal fluctuation in count and motility was made by using the ranking system shown in Table I. Post-operative readings represent the seminal findings six months after ligation. All samples were produced by coitus interruptus after three days' abstinence from intercourse.

TABLE I.—*Method of Ranking Sperm Counts and Motility*

Rank No.	Sperm Count (millions/ml.)	Rank No.	Active Motility
1	Over 60	1	Over 50%
2	21–60	2	11–50%
3	6–20	3	Under 11%
4	Under 6		
5	Azoospermia		

Results

Overall Effect on Fertility.—Before operation all cases were judged to be subfertile, because of a low sperm count or poor motility or both. Within six months of ligation, 67 cases (83.7%) were judged to be fertile (63 having vastly improved seminal rankings, and 4 producing a pregnancy without further analysis). Eight cases (10%) improved to higher seminal rankings but not to acceptably fertile levels. Four cases (5%) remained in their original ranking, and one case dropped to a lower rank.

Effect on Sperm Count.—Serial analyses over many months showed that the sperm count invariably rose slowly and steadily for as long as two years. Two such cases are cited by way of example:

G. F., aged 29, had a pre-operative sperm count of 5 million/ml. Six months after varicocele ligation the count had risen to 21 million, and at the end of two years it was 126 million.

D. C., aged 26, had a pre-operative sperm count of 0.25 million/ml. Four months after ligation it had increased to 32 million, and, at the end of a year, it was 62 million.

As shown in Table II, 50 out of 72 cases with a pre-operative sperm count ranking of 2 or more improved to a higher rank within six months; 21 cases were still in the same rank; and one case dropped to a lower rank. Changes in the sperm counts of men with very severe pre-operative subfertility or complete sterility are shown in Table III, which demonstrates plainly that the improvement is much greater than could possibly be accounted for by "normal fluctuation." These readings were taken at six months; many of them were much higher at a later date.

TABLE II.—*Sperm Count Rankings Before and Six Months After Varicocele Ligation*

Before Operation		After Operation				
Sperm Count Rank	No. of Cases	No. of Cases in each Rank				
		1	2	3	4	5
1	16	16				
2	30	16	13	1		
3	17	7	8	2		
4	19	3	6	7	3	
5	6		1	1	1	3

TABLE III.—*Effect of Varicocele Ligation on Cases of Azoospermia and Gross Oligospermia. (All Sperm Counts Expressed in Millions per ml.)*

Case No.	Pre-operative Sperm Count	Post-operative Sperm Count	Case No.	Pre-operative Sperm Count	Post-operative Sperm Count
1	Azoospermia	38	14	2	9
2	,,	14	15	2	8
3	,,	0·5	16	2	7
4	,,	Azoospermia	17	2	2
5	,,	,,	18	3	55
6	,,	,,	19	3	13
7	0·25	32	20	4	70
8	0·25	15	21	4	46
9	0·25	3	22	5	87
10	0·5	55	23	5	42
11	0·5	35	24	5	21
12	0·5	5	25	5	5
13	2	15			

Effect on Sperm Motility.—A visible improvement in the quality of sperm motility was the most striking feature of the post-operative analyses. Table IV shows, however, that there was also a significant improvement in the percentage of active sperms; no fewer than 48 of the 57 cases whose pre-operative motility was persistently under 10% had a post-operative activity of 50% or better within six months.

Effect on Pregnancy Rate.—This effect, so far as the patient is concerned, is the supreme test of success or failure of the operation, but it is appreciated that production of a successful conception cannot, by itself, be used as a yardstick to measure the value of any subfertility treatment as there are too many factors in *both* partners that must be taken into account. The seminal changes in 23 post-operative pregnancies are shown in Table V. All these cases had failed to produce

TABLE IV.—*Sperm Motility Rankings Before and Six Months After Varicocele Ligation*

Before Operation		After Operation		
Sperm Motility Rank	No. of Cases	No. of Cases in Each Rank		
		1	2	3
1	7	7		
2	18	13	5	
3	57	40	8	9

TABLE V.—*Seminal Changes in 23 Men Whose Wives Became Pregnant After Varicocele Ligation*

Case No.	Months Married Without Contraception	Months Between Ligation and Conception	Before Operation		After Operation	
			Count Rank	Motility Rank	Count Rank	Motility Rank
1	122	24	3	3	2	1
2	120	6	2	3	1	2
3	84	3	1	2	1	1
4	72	2	3	2	3	2
5	72	3	2	3	1	1
6	60	11	3	3	1	1
7	62	5	2	3	2	1
8	64	3	3	2	1	1
9	49	3	1	3	1	1
10	48	4	2	3	1	1
11	47	5	2	3	1	1
12	44	6	4	3	2	1
13	37	4	4	3	3	2
14	35	3	2	2	1	2
15	29	8	1	3	1	1
16	27	5	3	3	2	1
17	26	3	2	3	2	3
18	24	9	3	2	1	1
19	51	4	2	3	Not received	
20	50	4	2	2	,,	
21	37	3	3	3	,,	
22	26	12	3	3	,,	
23	84	3	2	3	,,	

a pregnancy for more than two years without recourse to contraception. This period of "barren marriage" was chosen because Tietze (1956) has shown that under similar circumstances in the United States 91% of first conceptions would be expected to have occurred. It is therefore considered significant that within a few months of varicocele ligation 29% of these subfertile men had successfully impregnated their wives; although it is freely admitted that two of them showed no post-operative improvement (Cases 4 and 17) and one was still below the acceptable fertile level (Case 13).

Discussion

Although many American and Continental seminologists still fail to accept varicocele as a contributory factor to male subfertility, there is now, in my opinion, ample evidence to the contrary, although the exact mechanism is not yet clearly understood. There is considerable evidence to suggest that the seminal changes are produced by increased intrascrotal temperature (Hanley, 1957). However, as similar high intrascrotal temperatures accompany large hydroceles, and as I have never been able to demonstrate any adverse effect on fertility in such cases, the increased temperature may only be an incidental finding. An alternative explanation may be that the damage is trophic in origin, due to some reversible type of reflex alteration in the calibre of the nutritional vessels (Harrison, 1958), because I have previously shown (Scott, 1958b), from testicular biopsy studies, that the tubular changes are bilateral although the varicocele is general unilateral.

The criteria for elective surgery (Scott, 1960b) demand careful selection of cases, the principle contraindications being previous disease of the opposite testis, particularly mumps orchitis (Scott, 1960c), and maldescent (Scott, 1961).

Whatever the explanation, a profound improvement occurs in the vast majority of cases, and a significant increase in the pregnancy rate can also be anticipated provided the patient's wife is fertile; if she is sterile there is no indication for operating on the husband.

Summary

The overall effects of varicocele, together with specific effects on the sperm count and motility, have been discussed. Significant post-operative improvement has been demonstrated in the sperm count in 78% of the cases, and in sperm motility in 81% of the cases; while the overall fertility was significantly improved in 83%. A pregnancy rate of 29% was achieved within a few months of operation. Possible mechanisms of the effect of varicocele on spermatogenesis are briefly discussed. The use of a ranking system for comparison of the pre- and post-operative seminal factors has clearly demonstrated that the changes after varicocele ligation are significantly greater than could be accounted for by normal fluctuation.

I thank my senior colleague, Mr. W. S. Mack, for his unfailing support and constructive criticism throughout the five years of this study.

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Leprosy: its Challenge and Hope, by Dr. R. G. Cochrane, has recently been published by the Mission to Lepers, and may be obtained from them at 7 Bloomsbury Square, London W.C.1, price 1s., or 1s. 4d. by post. The booklet covers the history of the disease, the position as it is to-day, and what measures can be taken to prevent and treat leprosy, all aspects being presented against a specifically Christian background. Dr. Cochrane is technical medical adviser to the American Leprosy Mission, Inc., and adviser on leprosy to the Ministry of Health, London. He was formerly director of the Christian Medical College, Vellore.

COMPARISON OF SUBJECTIVE AND OBJECTIVE ASSESSMENT OF ANGINA PECTORIS

BY

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Assessment of the severity of a patient's symptoms over a period of time is essential if the natural history of a disease and its response to treatment are to be studied. The patient may be asked to make this assessment for himself, or some aspect of his symptoms may be measured objectively. I report here the results obtained by these two methods in a small group of patients with angina pectoris, in order to draw attention to the lack of correlation between subjective and objective assessment in this condition.

The Investigation

Eleven patients (ten male and one female) were studied. There was an unequivocal clinical history of angina pectoris and an abnormal electrocardiogram at rest or after exercise in every case. These patients with angina pectoris formed part of a larger group with other manifestations of ischaemic heart disease in whom the metabolic effects of a diet rich in polyunsaturated fats was being studied. They were all on a diet containing no animal fat, were taking supplementary corn oil 1–3 oz. (28–85 ml.) a day, and were attending regularly for serum lipid analysis.

Case 1.—Man aged 55. Familial hypercholesterolaemia with cutaneous and tendinous lesions. Developed angina pectoris March, 1956.

Case 2.—Man aged 47. Angina pectoris began April, 1956.

Case 3.—Man aged 39. Onset of effort angina in May, 1958.

Case 4.—Man aged 40. Familial hypercholesterolaemia with skin and tendon deposits. Angina developed 1954.

Case 5.—Man aged 52. Angina pectoris began in 1952. January, 1954: anterior myocardial infarct, treated by bed rest and short-term anticoagulant therapy. Angina reappeared when he resumed normal activities.

Case 6.—Man aged 44. Developed angina pectoris in 1957.

Case 7.—Man aged 62. Angina pectoris since 1957.

Case 8.—Woman aged 61. Pernicious anaemia and early subacute combined degeneration of the cord 1950. Complete remission on vitamin B_{12}. 1952: posterior myocardial infarction. Angina of effort thereafter. 1957: found to have xanthelasma palpebrarum and tendon deposits. Serum cholesterol elevated.

Case 9.—Man aged 63. October, 1957: posterior myocardial infarction. Effort angina thereafter.

Case 10.—Man aged 60. Myocardial infarction March, 1957, and on resuming normal activities began to have angina pectoris.

Case 11.—Man aged 38. Effort angina from 1954. E.C.G. showed old posterior infarct. December, 1957: chest pain at rest, lasting several hours. Did not seek medical advice, but continued at work, and four days later had 10 teeth extracted under local anaesthesia. Died suddenly six hours later. Necropsy showed old posterior and recent massive antero-septal infarction.

The patients were seen every three to six months, and at each visit the severity of their symptoms was assessed subjectively and objectively.

Subjective Assessment.—The patients were asked about the frequency and duration of attacks of chest pain and the amount of exertion needed to produce them. They were also asked about such activities as cycling, gardening, household chores, running for buses, and so on. These points were discussed and recorded at each visit, and at the most recent interview they were asked to say whether, over the period of observation, they felt that they were "improved," "unchanged," or "worse."

Objective Assessment by a Standard Exercise Test.—A strong and stable wooden platform 18 in. (46 cm.) high, with a step at each end 9 in. (23 cm.) high, was used. A circular path, 10 walking paces long, was marked out on the floor from one end of the platform round to the other. The test was always done at 10–11 a.m., and therefore bore a constant relationship to meals. Comparable clothing was worn on each occasion, and for at least 15 minutes before the test the patients had been sitting quietly in the comfortably warm room where the test was done. The patients walked round the circuit at 100 paces a minute, in time to a metronome, climbing up the two 9-in. (23-cm.) steps on to the platform, down two 9-in. (23-cm.) steps, and walking 10 paces round to the steps again. When chest pain developed, the test was stopped and the time from the start to the onset of pain recorded. The time for the pain to pass off again was also noted, both measurements being taken, to the nearest five seconds, from a stop-watch. The patients could not see the stop-watch and were not told what their performance had been.

Body weight was recorded at each visit, and there was no significant change in any patient.

Results

Eight patients thought that they had improved during the period of observation and dietary treatment, and the other three felt that their condition was either unchanged or worse.

The results of the exercise tests are shown in Table I. Of the eight patients who believed that their effort tolerance was "improved" only three had better performances, the other five being unchanged or worse. Of the three patients who felt the same or worse, only one gave this result on the exercise test, the other two having improved their performance. Table II compares the subjective and objective assessments and shows agreement in four patients and disagreement in seven.

Discussion

In many chronic diseases such as asthma, bronchitis, and rheumatoid arthritis the patient's own assessment of his progress has been found to bear little relation to objective measurements of respiratory efficiency, strength of grip, and so on.

Fife *et al.* (1957) felt that this might also apply to patients with angina pectoris, and commented that "many patients will, of their own accord, modify their lives according to their exercise tolerance. . . . A substantial proportion adapt themselves to their disability in this way, and even in the absence of therapy may complain less of their symptoms as time passes, though questioning in detail will often elicit the fact that the degree of exertion required to induce the pain has not appreciably changed."

The discrepancy between the patient's exercise tolerance and his own assessment of it is clearly of

TABLE I.—*Results of Exercise-tolerance Tests in* 11 *Patients with Angina Pectoris*

Exercise Tolerance Improved						Exercise Tolerance No Change or Worse					
Case No.	Date	Pain On		Pain Off		Case No.	Date	Pain On		Pain Off	
		min.	sec.	min.	sec.			min.	sec.	min.	sec.
		Subjectively Improved									
1	25/3/58	6	0	—	40	4	8/11/57	2	20	—	40
	24/6/58	8	20	—	45		24/3/58	3	0	—	40
	2/2/59	10	0		40		6/6/58	2	40	—	25
	18/8/59	12	5		35		17/11/58	2	20	—	20
	16/6/60	11	10		30		21/5/59	3	0	—	30
							20/2/60	3	10	—	40
2	19/6/57	3	30	1	30						
	24/7/57	3	10	1	10	5	10/11/58	2	20	—	45
	7/1/58	6	0	1	30		18/2/59	3	10	—	40
	21/9/58	9	30	1	10		6/7/59	2	40	—	30
	3/1/59	10	0	—	40		6/1/60	3	5	—	45
	6/7/59	14	0	—	55						
	2/2/60	9	45	—	50	6	15/7/57	12	0	1	0
							7/11/57	5	0	1	30
3	17/11/58	7	0	—	25		24/3/58	5	25	1	20
	2/5/59	10	15	—	30		10/11/58	6	15	1	0
	17/8/59	12	5	—	35		6/7/59	5	40	1	15
	27/2/60	16	10	—	40		2/3/60	6	10	1	10
						7	9/8/57	3	50	—	45
							11/12/57	2	50	—	55
							5/5/58	3	40	1	40
							10/9/58	3	20	—	20
							21/1/59	3	30	—	20
							11/5/59	3	20	—	30
							29/9/59	3	40	—	35
							24/2/60	2	50	—	15
						8	26/9/57	4	30	—	40
							7/1/58	5	10	—	50
							20/8/58	5	30	—	30
							5/5/59	5	10	—	50
							17/2/60	4	55	—	40
		Subjectively No Change or Worse									
9	1/10/58	2	30	—	40	11	26/6/57	3	20	1	10
	9/1/59	4	40	—	25		20/10/57	2	0	—	50
	8/4/59	9	30	—	20		4/11/57	1	5	1	10
	8/7/59	9	20	—	30						
	17/2/60	8	20	—	15						
10	6/6/58	4	20	—	45						
	10/9/58	4	10	—	40						
	19/1/59	6	20	—	35						
	6/7/59	9	35	—	50						
	17/2/60	8	55	—	35						

TABLE II.—*Comparison of Subjective Assessment with Exercise-tolerance Test in a Group of* 11 *Patients with Angina Pectoris*

Subjective Assessment	Exercise Tolerance Improved	Exercise Tolerance No Change or Worse	Total
Improved ..	3	5	8
No change or worse ..	2	1	3
Total	5	6	11

first importance in therapeutic trials in angina pectoris, where remarkable subjective improvement tends to occur when any treatment is begun. Evans and Hoyle (1933) found that 38% of a group of patients given a placebo reported improvement in their angina, and an uncontrolled trial of any drug is therefore valueless. If, however, a double-blind trial is undertaken, and there are a substantial number of patients in both the control and test groups reporting improvement when their condition is unchanged, this could obscure a significant difference between the placebo and the drug on trial. Assessment by an exercise-tolerance test would undoubtedly overcome some of these difficulties if care is taken to standardize the conditions of the test. In particular, it is important to ensure that the rate of walking, the time interval from the last meal, the amount of clothing worn, and the room temperature remain constant throughout, and the patient should always be allowed to rest for at least 15 minutes before the test is done (Wayne and Laplace, 1933; Wayne and Graybiel, 1934).

It has been held that to exercise a patient until he gets pain is an unjustifiable risk; but, as Wayne and Laplace (1933) point out, "he is asked to do no more while under close control than he is in the habit of doing several times a day without supervision."

Summary

The progress of 11 patients with angina pectoris was assessed subjectively and by a standardized exercise-tolerance test. There was agreement between the two methods in only four patients, and disagreement in the other seven.

The implications of this finding with regard to therapeutic trials in angina pectoris are discussed.

I am grateful to Sir George Pickering for advice and encouragement.

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CLINICAL EVALUATION OF PHENIPRAZINE IN ANGINA PECTORIS

BY

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The use in angina pectoris of drugs which inhibit monoamine oxidase is a problem of current therapeutic interest. Conflicting reports on the use of one such compound, iproniazid, have been obtained; considerable success was claimed by Cossio (1958), Master (1958), and Towers and Wood (1958); but little therapeutic effect was found by Dewar *et al.* (1959) and Snow and Anderson (1959). The use of iproniazid is, however, limited by its toxic effects. A preliminary report on a similar monoamine oxidase inhibitor, pheniprazine hydrochloride (beta-phenylisopropylhydrazine; "cavodil"), which apparently has no toxic effects, was very encouraging (Mackinnon *et al.*, 1960), but little objective evidence was presented to support the conclusions. In view of this it was decided to carry out a controlled study of the clinical value of pheniprazine as a long-acting coronary vasodilator in patients suffering from angina pectoris.

Patients and Methods

Twelve out-patients aged from 49 to 70, with well-authenticated and typical features of angina pectoris, were studied. The angina had been static for the previous 12 months. There were nine men and three women, and in all of them the presumptive aetiology was coronary artery disease; one woman aged 43 (Case 11) had familial hypercholesterolaemia. Four patients had electrocardiographic evidence of previous myocardial infarction. All patients were taking trinitrin freely for their anginal attacks.

A double-blind technique was employed. An initial control period of one month was allowed when no additional coronary vasodilators were taken apart from trinitrin. One month's supply of either pheniprazine or an identical placebo was provided, neither the patient nor the observer knowing which drug was given. Two tablets of 3 mg. each were administered twice daily.

The patient was also given a specific number of trinitrin tablets. All patients attended at monthly intervals, and at each visit the number of trinitrin tablets consumed in the previous month was checked by the observer, thus ensuring an objective assessment of the number of anginal attacks. In addition, exercise-tolerance tests were carried out at the beginning of the study and at monthly intervals. The test was a modification of the two-step technique: the patient stepped up and down two steps, each 1 ft. (30 cm.) high, being timed on each occasion until the patient was stopped by either angina or dyspnoea. A note was made of the number of circuits undertaken and the time taken. An electrocardiogram was recorded before starting the exercise and immediately afterwards, using limb lead II and lead V_6 simultaneously. Ischaemic changes were indicated by S-T depression of the type and timing described by Wood (1956). Only one patient (Case 6) was unable to undergo the exercise-tolerance tests.

Results

Table I indicates the weekly number of trinitrin tablets taken during the control period and while the patients were on pheniprazine and the placebo. In eight patients both pheniprazine and placebo produced a fall in trinitrin consumption: but in only two of these did the fall with pheniprazine appreciably exceed that produced by the placebo (Cases 3 and 11). The remaining patients showed no change in trinitrin requirements with pheniprazine. The mean weekly consumption of trinitrin over the whole series was less with pheniprazine than in the control period: but the difference was not statistically significant. The trinitrin requirements during administration of the placebo also did not differ significantly from either the control period or while the patients were on pheniprazine.

The results of the exercise-tolerance tests are shown in Table II. The mean number of circuits undertaken while on pheniprazine was significantly greater than in the control period ($P<0.02$). An increase was also evident with placebo, but this was not significant, nor was there any significant difference between the performance with pheniprazine and that with the placebo. The rate of exercise did not vary significantly in the control period and during administration of pheniprazine and placebo. Table III shows that ischaemic changes were present after exercise in the electrocardiograms of eight patients while on pheniprazine—in three of these patients not showing ischaemic changes after exercise during the control period the S-T depression appeared after pheniprazine.

TABLE I.—*Weekly Consumption of Trinitrin During Control Period and During Administration of Pheniprazine and Placebo*

Case No.	Age	Sex	Duration of Angina	No. Trinitrin Tablets per Week		
				Control Period	Pheniprazine	Placebo
1	64	F	10 years	22	9	11
2	51	M	3 ,,	15	9	10
3	58	M	14 ,,	61	24	39
4	49	M	2 ,,	23	19	18
5	65	M	9 ,,	10	13	11
6	54	M	3 ,,	16	5	5
7	62	F	11 ,,	22	13	12
8	56	M	7 ,,	14	18	22
9	58	M	2 ,,	14	15	16
10	62	M	8 ,,	30	35	96
11	43	F	13 ,,	35	3	10
12	57	M	5 ,,	42	29	18
			Mean	25·3	16·0	22·3
			Standard error	4·3	2·8	7·2

TABLE II.—*Results of Exercise-tolerance Tests*

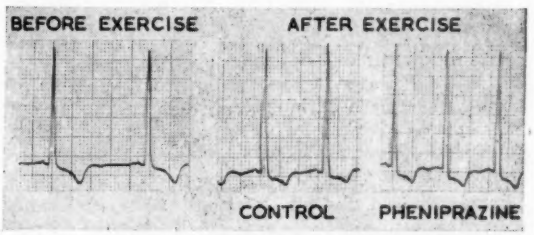
Case No.	Total No. of Circuits			Mean Time per Circuit (sec.)			Cause of Stopping		
	Control Period	Pheniprazine	Placebo	Cont.	Phen.	Pl.	Cont.	Phen.	Pl.
1	9	32	27	8·3	2·0	6·1	A	A	A
2	31	70	63	2·7	2·4	2·4	A	A	D
3	27	28	25	3·3	2·7	5·4	A	A	A
4	20	28	26	3·8	2·5	2·9	A	A	A
5	35	40	38	3·0	2·3	4·1	A	A	A
7	—	23	12	—	4·8	12·1	—	D	A
8	—	40	21	—	1·8	2·1	—	D	D
9	16	30	21	3·4	2·8	2·6	D	D	A
10	—	14	—	—	4·3	—	—	A	—
11	17	40	10	3·0	3·0	3·5	A	A	A
12	13	41	35	2·3	1·9	1·7	A	D	D
Mean	21·0	35·1	27·8	3·7	2·8	4·3			
S.E.	2·9	4·3	4·8	0·7	0·3	1·0			

A = Angina pectoris. D = Dyspnoea.

TABLE III.—*Progress of Ischaemic Changes in the Electrocardiogram*

Case No.	Presence of Ischaemic Changes		
	Control Period	Pheniprazine	Placebo
1	+	++	+
2	+	+	+
3	++	++	++
4	++	+	+
5	+	+	+
7	Not done	+	0
8	,,	++	+
9	,,	++	+
10	Not done	++	Not done
11	+	+	,,
12	+	++	,,

One patient (Case 1) expressed great satisfaction with pheniprazine and did show an improvement in the amount and rate of exercise; but the electrocardiographic changes of ischaemia became more pronounced, presumably because of the increased exertion (see Fig.). One other patient (Case 3) also experienced considerable subjective relief with pheniprazine, but no corresponding improvement was evident in exercise-tolerance tests.



Increase in ischaemic change during the exercise-tolerance test after administration of pheniprazine.

Only one patient had minor abdominal discomfort with pheniprazine. No consistent changes in pulse, blood-pressure, or weight occurred and no other side-effects were encountered with the drug.

Discussion

It has been stated that in the administration of any anti-anginal drug the therapeutic effect is directly related to the personality of the physician and his own belief in the curative powers of the drug, together with the suggestibility of the patient and the intensity of the patient's desire to be cured (Greiner *et al.*, 1950). This view is supported by Cole *et al.* (1958), who studied the effects of four coronary vasodilators in cases of angina pectoris and found a decrease in the frequency of chest pain in every patient regardless of whether an active drug or a placebo was being administered. The

importance of a double-blind technique in the investigation of an anti-anginal agent is therefore plain. More important still is the objective index of improvement provided by the electrocardiogram during a standard exercise-tolerance test.

Mackinnon *et al.* (1960) found considerable improvement with pheniprazine in 41% of 28 patients; but the improvement was assessed solely on subjective criteria —that is, on frequency of anginal attacks. In the present study there was a fall in trinitrin requirements with both pheniprazine and the placebo, in accordance with the findings of Cole *et al.* (1958); but there was no significant difference in the frequency of angina with administration of pheniprazine and placebo. The exercise-tolerance tests did show a significant increase in the amount of activity possible with pheniprazine, although the rate of performance did not alter. This apparent improvement was not, however, reflected in the electrocardiographic findings after exertion. In fact, the increased exertion produced an increase in the severity of ischaemic pattern in three patients. The primary action of pheniprazine is as an antidepressive agent, and it is possible that the resulting euphoria was responsible for the great improvement claimed by two patients, and may also have produced the increase in activity during the exercise-tolerance tests. However, the potential hazards of increasing exertion in patients with angina pectoris without a corresponding improvement in myocardial blood supply are obvious, and were well exemplified by the electrocardiographic changes in several patients during the course of the present study.

Summary

An objective study has been made of the clinical effect of a new monoamine oxidase inhibitor, pheniprazine hydrochloride (beta-phenylisopropylhydrazine; "cavodil"), in 12 patients with angina pectoris, using a double-blind technique.

No significant change in the frequency of anginal attacks followed the administration of the drug. Pheniprazine did, however, produce an increase in amount of exertion undertaken during exercise-tolerance tests; but the potential hazards of this in the absence of a corresponding increase in myocardial blood supply are pointed out.

It is concluded that pheniprazine is of no real value in treating angina pectoris and may, in fact, be contra-indicated.

My thanks are due to Dr. D. Verel for his helpful advice, and to the electrocardiographic technicians of the Sheffield Region Cardiovascular Centre for their willing co-operation in this study. I am also indebted to Benger Laboratories Ltd. for the supply of cavodil.

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Preliminary Communications

Clinical Assessment of "Etrynit" for Angina Pectoris

For any drug to equal glyceryl trinitrate it must be shown to be as effective, as harmless, and as cheap: its effectiveness can be judged by the rapidity of onset and the duration of effect.

Glyceryl trinitrate is generally accepted as the drug of choice, both for the rapid relief of the pain of angina and to prevent it if taken just prior to exertion. Unfortunately, its evanescent action limits its usefulness and it is of no value if taken at prescribed intervals during the day. A new preparation, the trinitric acid ester of trimethylol propane ("etrynit"), has been studied in Scandinavia (Nordqvist, 1959) and found to be of clinical value, although no papers have yet been published. The drug is claimed to be as effective as glyceryl trinitrate in the treatment of acute attacks and to have a longer duration of action.

A controlled trial has therefore been carried out to compare etrynit with glyceryl trinitrate, and this paper is concerned only with the first claim—namely, the rapid relief of pain in the acute attack of angina.

METHOD

A double-blind controlled trial was organized, using apparently identical tablets containing glyceryl trinitrate 1/130 gr. (0.5 mg.) and etrynit 10 mg., and the results were assessed by the established technique of sequential analysis (Armitage, 1954; Snell and Armitage, 1957). Thirty-five ambulant patients were treated. They were attending a cardiac clinic and had angina of effort, diagnosed by reliable clinical stories, supported in 33 instances by electrocardiographic changes. No patients with mitral- or aortic-valve disease or anaemia were included. There were 20 men, aged 38 to 64, and 15 women, aged 42 to 70. The electrocardiogram was abnormal in all but two, the abnormalities being either those of old cardiac infarction (20) or "coronary insufficiency" (13). Five patients were receiving anticoagulants, and these were continued. All were familiar with the use of sublingual glyceryl trinitrate to abort acute attacks of pain and all had had that drug for at least one month before starting the trial.

Each patient was given two boxes, identified only by numbers, and was asked to use no therapy other than the tablets in one box completely before starting the second box. The tablets were taken sublingually, in halves if this proved potent enough, and each box lasted about a week. One box contained glyceryl trinitrate and the other etrynit, and the boxes were filled in random order by the use of Fisher and Yates's (1957) statistical tables. When both boxes had been used the patient returned to the clinic and recorded the number of the box which contained the tablets he preferred, together with any side-effects or other comments. Although it was not strictly necessary statistically, the entire experiment was then repeated, so each patient received four boxes of tablets in all. The result of this second experiment confirmed the findings of the first.

RESULTS

A sequential analysis chart with boundaries equivalent to 5% significance was prepared, and as each result became available the pharmacist was able to translate

the box number into the drug preferred. These preferences were then plotted on the chart to produce a line showing the progress of the experiment.

Of the 35 patients who were given the trial drug, eight were unable to decide between the boxes and five refused to complete the trial, leaving 22 who were able to state a preference between the drugs. On the chart the progress line broke out into the area indicating "no significant difference" after 17 preferences, and the trend continued by the remaining five preferences. Of the 22 patients, 12 preferred glyceryl trinitrate and 10 preferred etrynit.

The assessment of a new preparation in the treatment of angina is notoriously difficult, for it is judged essentially by its subjective effect. It is well known that some patients with angina will improve at the start of any new form of treatment even if the preparation is inert (Evans and Hoyle, 1933). It was noticeable that patients who, prior to the trial, had come to rely on glyceryl trinitrate were very unwilling to rate any other tablet as better than their usual one, and this led to 11 patients condemning the tablets in all four boxes as far inferior to glyceryl trinitrate: two of the boxes, of course, contained glyceryl trinitrate. On the other hand, two patients preferred all four boxes to their usual glyceryl trinitrate.

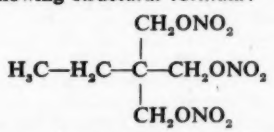
Although several patients commented that some of their boxes contained tablets with a much longer duration of action than usual, it was found, when the key was consulted, that this comment had been applied in equal numbers to etrynit and glyceryl trinitrate. This experiment was not designed to test the duration of action, and a trial is at present proceeding with this end in view.

Eight patients found all the trial tablets to be more rapidly effective than their usual glyceryl trinitrate, and this was because they were made up in a very rapidly disintegrating base. There was no significant difference in the time of onset of the two drugs used in the trial.

Side-effects.—Two patients complained bitterly of severe side-effects, in one case necessitating the patient going to bed and in the other causing him to go home from work. Both mentioned palpitation, nausea, and headache, and one also felt giddy. The tablet at fault was etrynit in one case and glyceryl trinitrate in the other. Five other patients complained spontaneously of headaches or palpitation with whole tablets, but in every case reducing the dose to half a tablet was effective. There was an equal incidence of side-effects with the two drugs and in this trial persistence of side-effects was not a problem.

DISCUSSION

Etrynit is a white crystalline substance readily soluble in acetone or absolute alcohol but insoluble in water. It has the following structural formula:



As etrynit is a nitrate ester it is likely that its mode of action is similar to that of glyceryl trinitrate, although hydrolysis in the body is probably slower. In animal experiments the actions of these two drugs on smooth muscle and on the coronary arteries appear to be identical.

On the isolated heart of the rabbit the time of onset, duration of action, and maximum effect are the same for glyceryl trinitrate and etrynit when doses are equal. Clinically, using forearm plethysmography on healthy test subjects, and a dose of etrynit five times greater than that of glyceryl trinitrate, the effect began at the same time with both preparations, but the maximum effect of etrynit was obtained later than that of glyceryl trinitrate and was more lasting. As measured by changes in the blood-pressure, the effect of etrynit occasionally lasted for five to seven hours (Nordqvist and Varnauakas, 1961).

In our clinical trial persistence of the action of etrynit was not commented on by our patients, but it is likely that as soon as the pain has been relieved they cease to notice any but the most unpleasant effect of the drugs, so that a prolonged action may pass unnoticed.

There are a few patients who genuinely cannot tolerate glyceryl trinitrate, and for these the availability of an alternative preparation of equal effectiveness in the acute attack should prove of great value. In view of the short duration of action of glyceryl trinitrate and the failure, in our opinion, of pentaerythritol tetranitrate or any other drug to prevent attacks or even to reduce their frequency or severity, if etrynit can be shown to be as effective as a preventive as we have found it in the acute attack it should prove a most valuable drug.

CONCLUSIONS

For the treatment of the acute pain of angina, etrynit is as effective as glyceryl trinitrate. The usual dose is 10 mg. sublingually, but in most cases 5 mg. is adequate.

The frequency of troublesome side-effects was low and was equally common with the two drugs, but with etrynit 5 mg. side-effects were less severe than with glyceryl trinitrate 1/130 gr. (0.5 mg.).

We feel that etrynit is worthy of further study, particularly with regard to its prophylactic action, as it is the only drug which has yet convinced us that it measures up to glyceryl trinitrate for the relief of the acute pain of angina.

We thank Dr. J. Rae, of Bayer Products, for the trial tablets, and Mr. D. Davenport, chief pharmacist, King's College Hospital, for his assistance.

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The Swiss Federal Government is paying half the cost of the medical studies of four young Congolese students (Léopoldville) who arrived from the Congo at the beginning of the 1960–1 academic year and are in the first year of their medical course at the University of Geneva. W.H.O. is assisting three students who are now attending the Medical Faculty at Lyons, and 60 medical assistants who had received some training in the Congo and are now following courses in the French universities of Lyons, Bordeaux, Rennes, Nantes, and Montpellier which will enable them to qualify in a minimum of three years. (WHO/6.)

Medical Memoranda

Rupture of Pregnancy in a Rudimentary Uterine Horn

Congenital anomalies of the uterus are caused by failure of fusion of the two Müllerian ducts, complete or partial persistence of the septum between them, or failure of one side to develop. The classification of such cases has been reviewed by Holmes (1956), who thinks they are more common in association with pregnancy than was formerly believed and estimates their incidence as about 1 in 1,000 pregnancies. One of the more frequently encountered of these abnormalities is uterus bicornis unicollis, vagina simplex. Pregnancy in such an organ may proceed normally where the myometrium of each horn is adequately developed, although delivery of the child may present difficulties (Rademaker and Royer, 1951; Falls, 1956). More rarely, however, one horn is rudimentary and thin-walled. Rupture during pregnancy will then almost inevitably occur, with a high risk of maternal death, because the cervical portion is largely fibrous and incapable of much dilatation. Occasionally the pregnancy will proceed without rupture: when labour ensues difficulty in expulsion results in death of the foetus (Lahmann, Kilkenny, and Mietus, 1941), and even its retention in a mummified condition for up to 20 years afterwards (Scott and Forman, 1916).

The following case is one in which rupture occurred.

CASE REPORT

An unmarried 20-year-old primigravida began her last menstrual period on July 14, 1959, her menses having been regular and normal. The pregnancy was uneventful until the evening of November 2, apart from a slight pinkish vaginal loss for the preceding three days. She then noticed mild lower abdominal pain and went to bed, but was awakened at 6 a.m. by severe colicky hypogastric pain which worsened and became constant. She later complained of "difficulty in breathing," fainted, and was doubly incontinent.

Examination at 10.15 a.m. showed an extremely pale shocked woman complaining of loss of vision on trying to sit up, and slight right shoulder-tip pain. "Air-hunger" was noted, with pulse 140, temperature 97.4° F. (36.3° C.), and B.P. 65/25. The abdomen was distended to the umbilicus, with dullness in both flanks. Vaginal examination disclosed a single softened closed cervix without bleeding; the size of the uterus could not be clearly defined.

A diagnosis of ruptured ectopic pregnancy was made, morphine, ¼ gr. (16 mg.), was given and an immediate intravenous infusion of dextran begun. On arrival at hospital, 15 miles distant, her general condition had improved and transfusion was continued with group O Rh-negative blood. At laparotomy the peritoneum was distended with 4–5 pints (2.3–2.8 litres) of blood. A four-months foetus was lying free in the abdominal cavity, having been extruded through a tear in the upper surface of a rudimentary left horn of a uterus bicornis unicollis to which the placenta was still attached. The round ligament arose lateral to the placental site. Both tubes and ovaries appeared normal: the right uterine horn was slightly enlarged. The rudimentary horn was removed by clamping, cutting, and ligating its attachment to the right horn, left tube, and round ligament.

Subsequent recovery was uneventful, the patient leaving hospital on the tenth day and returning to work on the twenty-seventh day after operation. Intravenous pyelography later showed a normal renal tract.

COMMENT

The diagnosis of pregnancy in a rudimentary horn prior to laparotomy presents considerable difficulties because, unlike uterus didelphys, the cervix is single and there is no vaginal septum to indicate that any congenital uterine abnormality is present. The usual clinical picture, as in the present case, is of a ruptured ectopic gestation with massive intraperitoneal haemorrhage (Saleh, 1955; Reyner and Wetchler, 1955). Unlike cases of tubal pregnancy in which rupture takes place before the ninth week, the catastrophe nearly always occurs during the fourth month or later, and pregnancy in a rudimentary horn should be suspected where this longer duration of amenorrhoea is noted. Latto and Norman (1950) reported one of the few cases in which a correct pre-operative diagnosis was made. Haemorrhage may be so severe that death occurs within 15 minutes (Mulsow, 1945). Rupture may occasionally be delayed as late as 36 weeks (Cody, 1958). Other cases have been reported by De Nicola and Petersen (1947), Garber and Kistner (1949), and Carpenter and Jameson (1952).

At operation the distinguishing feature from a tubal pregnancy is the attachment of the round ligament lateral to the gestation sac.

In many cases of uterine abnormality there is an associated congenital renal anomaly. None was found in the present case, unlike that of Lahmann *et al.* (1941), in which there was unilateral renal agenesis.

This report also illustrates the value of the rural practitioner being equipped with either plasma or a plasma substitute. The former is preferable, since synthetic colloid substances may cause difficulty in subsequent cross-matching of blood or contribute to afibrinogenaemia.

My thanks are due to Mr. Donald Beaton, who performed the operation, for his helpful criticism in preparing this report.

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The Oxford University Committee for the Advancement of Medicine says in its annual report for 1959 that "one of the most urgent needs, and one that is common to all, is adequate accommodation to deal with the increasing demands of the sick, both medical and surgical. The need is particularly for new operating theatres, up-to-date wards, and an out-patient department adequate for local, regional, and university needs. The situation is a grave one, for the medical and surgical staff at large are conscious that they are not caring for the sick in the way that they wish to do because of this inadequate accommodation. Nor, because of this shortage, is it often possible to admit patients for research purposes." (*Oxford University Gazette*, February 28, 1961.)

Reviews

MODERN CARDIOLOGY

Modern Trends in Cardiology. Edited by A. Morgan Jones, M.Sc., M.B., F.R.C.P. (Pp. 264+ix+13; illustrated. 70s.) London: Butterworths. 1960.

A book like this must be selective in such a vast and growing field as cardiology. The editor has organized a distinguished assembly of authors from the English-speaking world—including Sweden! The first half of the book deals with a mixture of topics—for example, cardiac metabolism, circulatory dynamics, respiratory function tests, pulmonary hypertension, renal function in heart disease, electrolytes in heart failure, treatment and prophylaxis, and cardiac surgery. The second half is entirely devoted to coronary disease, including chapters on epidemiology, metabolic factors, coronary flow measurements, diagnosis, prognosis, and treatment.

The reader will find little that is stereotyped, and without exception the various contributors deal with their subjects with critical erudition and up-to-date knowledge. The extensive section on coronary disease to some extent reflects not only the massive research but also the great perplexities and unanswered questions which still remain. Some of the communications are provocative and incisive (Sharpey-Schafer). Others contain very recent work based on the original researches of the authors (Bing, Werkö, Gorlin). Bedford, Holmes Sellors, and Campbell write from their rich experience in congenital heart disease. On the subject of coronary artery disease Oliver gives an excellent critical account of the relationship to lipid metabolism, while Hill gives a carefully balanced assessment of the place of diet and other measures in treatment. Both authors exercise commendable caution in their conclusions, presenting both sides of the debatable anticoagulant problem. Feil confuses an otherwise useful table on prognosis by the inclusion of survival figures from necropsy series. Gorlin's recent work on myocardial metabolism in heart failure will stimulate great interest, confirming for the first time in man Starling's suggestion that the oxygen consumption of the heart is closely related to its volume: as the filling pressure of the heart rises with failure the oxygen cost of the same cardiac work is increased. A revolutionary change in views on coronary disease is likely to follow the recent introduction of direct coronary angiography in man—too recent for more than brief mention in this monograph.

The impossibility of considering the heart and heart failure in isolation is recognized by the editor, who has called in his Manchester colleagues, Butler and Black, to deal with the lungs and electrolyte disturbances respectively. These are excellent chapters which should be fully studied and assimilated by clinical cardiologists who require this basic knowledge to approach a comprehension of the total disorder in patients with cardiac failure.

This monograph has great merit in being so nearly up to date. Many of the references have been published only in recent months. I came across only one unfortunate slip: W. M. Bayliss is referred to as Bailey—and by a British author at that!

This book is a most valuable addition to the Modern Trends series. Every cardiologist will find something of interest, and in fields outside his own research interest he will find descriptions of new work which are both clearly presented and exciting to contemplate.

J. McMICHAEL.

SUBMOLECULAR BIOLOGY

Introduction to a Submolecular Biology. By Albert Szent-Györgyi. (Pp. 135. $5.) New York and London: Academic Press. 1960.

"What drives life is thus a little electric current, kept up by the sunshine. All the complexities of intermediary metabolism are but lacework around this basic fact." No doubt, but what a triumph of exposition to convince the reader with no very special knowledge of redox potentials, electron affinities, orbital energies, and electron mobility that this broad simplification can be followed without too great effort. Those of us who are familiar with the juggling of energy between ADP and ATP and the role of the high-energy phosphate bonds in driving life must have wondered from time to time how such energy is converted into mechanical, electrical, or osmotic work. Well, this is what Szent-Györgyi tackles with great gusto and imagination, and it is really worth the sweat to go along with him even though there are plenty of tough obstacles that must be overcome and a gool deal of patience is needed for mastering the terminology.

All kinds of exciting ideas crowd the pages of this little book, which bear directly on the cellular interactions of riboflavin, serotonin, corticosteroids, the nature of ionic activity and "lyotropic series," and metachromasia, to mention a few examples.

Drug action is brought into the orbit of electron donation and acceptance. Chlorpromazine, for instance, looks as if it owes its unique properties to its qualities as electron donor. "And, if the symptoms of schizophrenia can be influenced favourably by electron donation, then, perhaps, a lack of electrons may be involved in the genesis of this disease, and if so, the question comes up: what has induced it?" All very well, the reader no doubt is thinking, but where does one go from here? Read Dr. Szent-Györgyi and find out, though you will suffer some disappointment and despair before you succeed. And that, precisely, is how this miracle of a book works.

The reviewer has enjoyed tackling the challenge of submolecular biology in the company of Szent-Györgyi and now looks forward to mastering another exciting discipline that may well revolutionize our ideas of cellular behaviour.

ROY CAMERON.

EFFECTS OF POLLUTION

The Effects of Pollution on Living Material. Symposia of the Institute of Biology. No. 8. Edited by W. B. Yapp. (Pp. 154+xii; illustrated. 25s.) London: Institute of Biology. 1959.

In public health problems which are frequently the subject of public and political controversy there is a constant tendency for the facts to be obscured by opinions. With the advance of scientific knowledge many sanitary or public health nuisances of former years are now known to be more aesthetic than actual sources of disease. When the drive to prevent disease by the removal of environmental pollution began in the mid-nineteenth century, the bacterial cause of infection was unknown and the miasmic theory was

still accepted. It is therefore highly desirable that the known effects of pollution should be clearly set out for study and for reference.

This volume is a report of the eighth symposium of the Institute of Biology held in September, 1958. It deals with the effects of various kinds of pollution in rivers and estuaries, atmospheric pollution, and the problems of environmental pollution by radioactive substances. To the medical reader with his particular interest in human ecology this book has much of interest, especially the chapters dealing with atmospheric pollution and radioactivity. Although the deleterious effects of atmospheric pollution, especially to the town dweller, have been known and condemned for some 300 years, it is surprising that the effects of dirty air on man are still so imperfectly understood. The excellent contributions on air pollution by Dr. E. T. Wilkins and Dr. P. J. Lawther reveal our lack of knowledge and the difficulties which still confront this country in the national effort for cleaner air.

The chapters on radioactivity give a readable account of the present knowledge on this subject, and Dr. Carter's contribution on the controversial subject of the genetic effects of radioactive pollution is worthy of study. It is a reasoned account based solely on scientific knowledge of the genetic hazards resulting from the world-wide uses of radioactivity. While the chapters on river and estuarial pollution are mainly of interest to biologists, the medical officer of health will find them worthwhile reading.

A. B. SEMPLE.

MEDICAL ETHICS AND THE ROMAN CHURCH

The Ethics of Medical Practice. By John Marshall, M.D., F.R.C.P.(Ed.), M.R.C.P.(Lond.), D.P.M. (Pp. 164. 21s.) London: Darton, Longman and Todd. 1960.

Most writers about medical ethics are content to describe a code of conduct which is generally acceptable to contemporary doctors of good repute without any reference to morals and philosophy. The author of this book is more courageous; in his first chapter he defines the basis of ethics as it appears to a devout adherent of the Roman Catholic Church, and, from this standpoint, he deduces some general principles and obligations of medical practice before embarking on a detailed discussion of such controversial matters as euthanasia, the transplantation of organs, the investigation of fertility, artificial insemination, sterilization, contraception, and abortion. For a Roman Catholic the morality of psycho-analysis is complicated by Freud's denial of the existence of original sin and his assertion that religion is no more than a comfortable illusion; the "practical solution" suggested—that a Catholic patient should be referred to a good psychiatrist who is also a good Catholic—must be difficult to achieve.

The fundamental problem, however, is whether there exists a "Natural Law" in the sense of St. Thomas Aquinas's description of "a knowledge naturally belonging to man by which he is guided to the right performance of the actions proper to him," or whether the human race in its evolution developed its sense of right and wrong by the slow growth of knowledge and inherited tradition, including the example of exceptional individuals. Varying standards in different races in different situations at different periods of time suggest that the sense of right and wrong may be an acquired rather than an inborn character. St. Augustine's definition of natural law as "the divine reason or will which enjoins the preservation and forbids the disturbance of the natural order" might, if construed literally, be held to forbid any treatment of disease, because sickness, accident, and death are surely part of the natural order. Since the scientific revolution human activity has involved much control and disturbance of the forces of nature, and most of those who enjoy the amenities of civilized life would be reluctant to surrender them or believe that they are contrary to any natural law.

The writing of this book is clear and simple. The opinions expressed are definite, and though many doctors will be unable to accept all the reasoning as valid they may be grateful for the candour and obvious sincerity with which the attitude of the Roman Church is defined to the many problems that scientific progress presents to traditional belief, and some interesting examples are recorded of change in theological opinion as a consequence of it.

A. P. THOMSON.

TUMOURS OF THE CALVARIA

Primary Tumors of the Calvaria: With Special Consideration of the Clinical Problems. By Franklin Jelsma, M.D. (Pp. 116+x; illustrated. 56s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1960.

In this short monograph emphasis is laid on the clinical aspects of skull tumours, with particular reference to their diagnosis and treatment. The author has had more than average experience of the subject, and the work is almost entirely based on his own clinical material. He has interpreted the term "primary tumours" very widely, so that we find among them conditions as diverse as Paget's disease and a leptomeningeal cyst associated with a partial cranial defect. The calvaria is that part of the skull above a line linking the superior orbital ridges and the superior nuchal line of the occipital bone; this limitation excludes tumours of the base of the skull. This is unfortunate, because it limits the usefulness of the work as a source of reference for the clinician.

Differential diagnosis is one of the major difficulties in the evaluation of a clinical problem, and greater emphasis could have been laid on this aspect, particularly in connexion with the radiological appearances. The differential diagnosis of various bone defects might have been clarified by a series of illustrations. This could well have been done at the expense of a number of case histories which appear to have been included for no purpose other than the completion of the clinical descriptions of the entire series, which are in any case summarized in a table. It is debatable whether or not some of the intradiploic traumatic cysts were in fact ossified subperiosteal haematomas, particularly in the case included as an addendum, and it is even more questionable whether hyperostosis frontalis interna was responsible for the symptoms described in four cases.

The need for such a work is appreciated, but the scope of this volume could be more comprehensive. The section on haemangiomas of the skull is useful, and valuable advice is given on the surgical treatment of the various lesions described. There is a good bibliography.

P. H. SCHURR.

ORTHOPAEDIC LECTURES

Instructional Course Lectures. Volume XVI. 1959. American Academy of Orthopaedic Surgeons. Editor Fred C. Reynolds, M.D. (Pp. 335; illustrated. £6.) St. Louis, Missouri: C. V. Mosby Company. 1959.

This is the sixteenth volume of selected lectures given at the instructional courses sponsored by the American Academy of Orthopaedic Surgery. The publication of these lectures, inaugurated by Dr. J. E. M. Thomson, was assured of success from the beginning of 1943. This volume includes a symposium on injuries to athletes, selected lectures on the hand, foot, and knee, unequal extremities, and the spine, with a section on fractures largely devoted to the use of a prosthesis for the treatment of fresh fractures of the femoral neck. The editor has chosen subjects of contemporary interest, and each lecture is of sufficient importance to be read as an entity, for the volumes are not intended to form a textbook.

The treatment of claw hand is described, use being made of various tendon transfers developed by Bunnell, Fowler, and others for paralytic conditions. For Dupuytren's contracture subcutaneous fasciotomy under local analgesia is favoured. The conservative and operative treatment of club foot is discussed. "Medial release" is advised when failure of closed methods is recognized, and this is advocated between the ages of 3½ and 5½. The long article on the role of subtalar fusion in the treatment of valgus deformity of the foot is full of information. The author uses bone grafts, holding that this procedure is useful for the growing child to maintain an arch while the foot develops, and he appreciates that triple arthrodesis is required in some feet later. A lecture on electromyography in orthopaedic surgery should be read. The symposium on the treatment of fresh fractures of the neck of the femur reports the experience at eight clinics, with an excellent summary by Dr. J. E. M. Thomson. Stewart has experience of 300 and Moore of 135 operations for fresh fracture using a prosthesis. The general feeling appears to be that results are encouraging, particularly when Moore's vitallium prosthesis is employed, but that experience is still insufficient to advocate definite indications for the procedure. The 260 excellent illustrations are well chosen from radiographs, photographs, and line drawings. These lectures will be invaluable to the postgraduate student.

ST. J. D. BUXTON.

BRONCHOVASCULAR ANATOMY

Surgical Anatomy of the Bronchovascular Segments. By William E. Bloomer, M.D., Averill A. Liebow, M.D., and Milton R. Hales, M.D. Foreword by Gustaf E. Lindskog, M.D. (Pp. 273+xi; illustrated. £6 12s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1960.

This extremely well produced volume on bronchovascular segments consists largely of photographs and diagrams taken from casts of the bronchial tree with the object of demonstrating the finer points of surgical anatomy, not only of the bronchi themselves, but also of their related blood-vessels. A section on angiography is also included showing that the casts are not gross distortions of the normal anatomy.

Surgeons who are undertaking segmental and lobar resections will find this a valuable book of reference, though the variations described and illustrated will not be unexpected. The reader may find a certain amount of difficulty in accepting a letter and numerical definition of the various bronchi, and following the pattern introduced by Boyden may encounter a little difficulty in deciding what bronchus BX^1b represents, and, similarly, the recognition of the vessel V^3d may require a few minutes' thought.

There is undoubtedly a wealth of information contained in this atlas, but in its practical application there is almost an excess of detail which is not likely to concern the operating surgeon.

T. HOLMES SELLORS.

HUMANE ANIMAL EXPERIMENTS

The Principles of Humane Experimental Technique. By W. M. S. Russell, M.A.(Oxon.), D.Phil.(Oxon.), and R. L. Burch. (Pp 238+xiv; illustrated. 30s.) London: Methuen and Co. Ltd. 1959.

This book is founded on a report made in 1958 to the Universities Federation for Animal Welfare. It embodies systematic work by the authors on the progress of humane technique in the laboratory in the United Kingdom. The problem set to the authors resolved itself into the conflict between experimental biology (including medicine) on the one hand and "humanity" on the other. The use of this latter word—and its opposite, "inhumanity"—has involved the authors in writing a footnote explaining that it is used in its secondary sense of "humaneness." The principle is put forward that successful animal experimentation has the prerequisite of humane technique.

The book divides into two parts, the scope of humane technique and its progress. The first part discusses the underlying philosophy of humanity and inhumanity, various aspects of animal experimentation in Great Britain, and the types of work requiring such techniques. All are regarded from the aspect of whether or not inhumane methods are utilized. In the second part the authors discuss at considerable length all the biological methods used in research from tissue culture to experimental psychiatry; they include the uses of mathematics to achieve increased accuracy, which often means that fewer experimental animals need be used. Finally, they consider the personality of the experimenter and the sociological factors which may make or mar progress in the use of humane techniques.

There are extensive tables and masses of facts; a good bibliography and limited illustrations. It is an essentially useful book, but, if the operator is not intrinsically humane in technique before reading it, one doubts whether it will convert him despite its patent desire to achieve this important and laudable end.

A. ST. G. HUGGETT.

ATLAS OF BLOOD CELLS

Atlas of Clinical Hematology. By Katsuji Kato, Ph.D., M.D. (Pp. 296; illustrated. £8 15s.) New York and London: Grune and Stratton. 1960.

In 1938 the author exhibited at a convention at San Francisco a collection of paintings and drawings of blood and bone-marrow cells made by himself for teaching purposes. This collection, with additions to bring it up to date, forms the material of this excellently produced volume. The plates represent composite pictures showing the various kinds of cell that may be met with in the condition illustrated; they do not, therefore, represent any single microscope field, however typical. On the page opposite each plate is a line diagram with a

key for identifying the cells. The book is divided into 50 sections each dealing with a different subject—for example, the blood in infants and children, acute leukaemia, nucleophagocytosis. Each of these sections is preceded by a brief discussion of the subject, which ends with a few key references; these references are mostly now of historical interest and there are few after the 1940's. The discussions, however, are contemporary. The 92 colour plates are exquisitely painted and the reproduction is first-class; the utmost care has clearly been taken to secure clear definition. The plates show the very best that can be obtained by these methods and the paintings show remarkably accurate detail in nuclear patterns and cytoplasmic structure, detail still beyond the definition of photomicrography. Every recognizable haematological condition is illustrated, including rarities like Niemann-Pick's disease and secondary neuroblastoma in the marrow. Conditions illustrated that have been more prominent since 1938 are the L.E. cell phenomenon, sex chromatin in polymorphs, and mast-cell leukaemia.

With improved teaching of haematology to undergraduate and postgraduate medical and technical students, atlases of this type tend to be less used, and the emphasis is more on illustrating individual cell-types and their variation with examples of actual microscopical fields. In this way the student can more easily identify the cells in specimens he is actually working over. Professor Kato is professor of physiology, and in that context atlases of his type have a place. His atlas is certainly one of the best of its kind, but its inevitably high price will tend to keep it a collector's piece, for the special department.

M. C. G. ISRAËLS.

BOOKS RECEIVED

Review is not precluded by notice here of books recently received.

Midwifery. By Ten Teachers. Under the direction of Frederick W. Roques, C.B.E., M.D., M.Chir., F.R.C.S., F.R.C.O.G. Edited by Frederick W. Roques, John Beattie, and Joseph Wrigley. Tenth edition. (Pp. 739+viii; illustrated. 45s.) London: Edward Arnold (Publishers) Ltd. 1961.

Man Against Aging. By Robert S. de Ropp. (Pp. 310. 21s.) London: Victor Gollancz Limited. 1961.

Pioneer Microbiologists of America. By Paul F. Clark. (Pp. 369+xiv. $6.) Madison: The University of Wisconsin Press. 1961.

Educacion Sexo y Sexualidad. By Dr. Carlos Colmeiro-Laforet. (Pp. 185. 150 pesetas.) Vigo, Spain: Tipografia. 1961.

Die Beurteilung der Zurechnungsfähigkeit. Ein Vortrag. By Kurt Schneider. (Pp. 33. DM. 2.70.) Stuttgart: Georg Thieme Verlag. 1961.

Classification of Kin, Age Structure and Marriage Amongst the Groote Eylandt Aborigines. A Study in Method and a Theory of Australian Kinship. By Frederick G. G. Rose. (Pp. 572+xii; illustrated. £5.) Oxford, London, New York, Paris: Pergamon Press. 1960.

Side Effects of Drugs. Unwanted Effects of Drugs as Reported in the Medical Literature of the World During the Period 1958-1960. Compiled by L. Meyler, M.D. (Pp. 239. No price.) Amsterdam, London, New York: The Excerpta Medica Foundation. 1960.

The Eye and Its Function. By R. A. Weale, Ph.D., D.Sc. (Lond.). (Pp. 209; illustrated. 55s.) London: The Hatton Press Limited. 1960.

From a Doctor's Diary. By Charles Vere Nicoll. (Pp. 179; illustrated. 16s.) Shrewsbury: Wilding and Son Ltd. 1960.

The Organization and Financing of Research in Biochemistry and Allied Sciences in Great Britain. Edited for the Biochemical Society by K. S. Dodgson. (Pp. 51. 2s. 6d.) London: Biochemical Society. 1960.

The Rickettsial Diseases. By P. F. Zdrodovskii and H. M. Golinevich. Translated from the Russian by B. Haigh, M.A., M.B., B.Chir. (Pp. 629+xii; illustrated. £5 5s.) Oxford, London, New York, Paris: Pergamon Press. 1960.

Narrative of a Child Analysis. The Conduct of the Psycho-Analysis of Children as seen in the Treatment of a Ten year old Boy. By Melanie Klein. (Pp. 496+74; illustrated. 75s.) London: The Hogarth Press and the Institute of Psycho-Analysis. 1961.

Silicosis and Other Pneumoconioses in Sweden. By Axel Ahlmark, Torsten Bruce, and Ake Nyström. (Pp. 398+xxx; illustrated.) Stockholm: Svenska Bokförlaget. 1960.

Biosynthese und Stoffwechselwirkungen der Schilddrüsenhormone. By Dr.-Ing. G. Hillmann. (Pp. 133+viii. DM. 26.50.) Stuttgart: Georg Thieme Verlag. 1961.

Fluorine and Dental Health. The Pharmacology and Toxicology of Fluorine. Edited by Joseph C. Muhler and Maynard K. Hine. (Pp. 201. 21s.) London: Staples Press. 1960.

Leucemie Basefile. By Nevio Quattrin, Enrico Dini, Emmanuele Palumbo. (Pp. 233; illustrated. L. 2,500.) Pisa: Omnia Medica. 1959.

Progress in Endocrinology. Part II. ***Biochemistry and Biological Actions of Steroids and Other Hormones. Proceedings of the Edinburgh meeting on Endocrinology. 16-20 August 1959.*** Edited by K. Fotherby, J. A. Loraine, J. A. Strong, and P. Eckstein. (Pp. 167+xi; illustrated. 45s.) Cambridge: The University Press. 1961.

Erkrankungen der Leber und der Gallenwege. Vols. 1 and 2. By Dozent Dr. I. Magyar. (Pp. 467; illustrated. Pp. 351; illustrated. No price.) Budapest: Verlag der Ungarischen Akademie der Wissenschaften. Berlin: Akademie-Verlag. 1961.

Air Pollution. By various authors. (Pp. 442; illustrated. Clothbound edition £2.) Geneva: World Health Organization. London: H.M. Stationery Office. 1961.

L'Entérésie. Étude clinique, diagnostique et therapeutique. By Dr. Michel Soule and Dr. Nicole Soule. (Pp. 132+viii. NF. 8.) Paris: Presses Universitaires de France. 1960.

Principles of General Neurophysiology Relating to Anaesthesia and Surgery. By Barry D. Wyke, M.B., B.S.(Sydney). (Pp. 136+ix; illustrated. 21s.) London: Butterworth and Company (Publishers) Ltd. 1960.

Fifth International Meeting of Biological Standardization held at the Hebrew University, Jerusalem, September 17-20, 1959. (Pp. 496+xiv+xvi. No price.) Israel: Weizmann Science Press. 1960.

Les Suppurations Bronchiques, Pulmonaires et Pleurales. By Raoul Kourilsky and Guy Decroix. (Pp. 259; illustrated. No price.) Paris: J.-B. Baillière et Fils. 1960.

D. Danielopolu. Opere alese. Edited by M. Milcu. (Pp. 497. No price.) Rome: Editura Academiei Republicii Populare. 1960.

Opera et Opuscula Collecta edidit Institutum Clinices Universitatis Upsaliensis. Volume XII–XIII, 1958–1959. Editor: Erik Ask-Upmark. (Pp. 152; illustrated. No price.) Uppsala: Almqvist and Wiksells Boktryokeri Ab. 1960.

Laennec. His Life and Times. By Roger Kervran, M.D. Translated from the French by D. C. Abrahams-Curiel. (Pp. 213+x. 21s.) Oxford, London, New York, Paris: Pergamon Press. 1960.

Mary Ann Goes to Hospital. By Mary Cockett. (Pp. 63; illustrated. No price.) London: Methuen and Company Limited. 1960.

Human Ecology and Health. An Introduction for Administrators. By Edward S. Rogers, M.D., M.P.H. (Pp. 334+xviii. 54s.) New York: The Macmillan Company. 1960.

Toward the Diagnosis of Congenital Heart Disease. By W. Carleton Whiteside, M.D., F.R.C.S.(C.), F.A.C.S., F.I.C.S., D.A.B.T.S. (Pp. 86+xii. 36s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications Ltd. 1960.

Quoi de Nouveau en Pratique Médicale 1960? By Prof. C. Lian and colleagues. (Pp. 384+xiii. 12.50 NF.) Paris: R. Lépine. 1960.

Medical Evidence in Personal Injury Cases. The Medico-Legal Aspects of an Action for Damages Arising out of a Personal Injury. By Dorothy Knight Dix and Alan H. Todd, M.S., B.Sc. London, F.R.C.S.Eng. (Pp. 242+xii; illustrated. 42s.) London: H. K. Lewis and Co., Ltd. 1961.

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VARICOCELE

Matters have progressed somewhat since the days when the three important features of a varicocele were said to be its occasional association with renal tumour, its disqualifying effect on attempted entry into the Services, and its spelling as "cele" and not "coele." Many conditions in fact previously accepted as being relatively harmless have latterly assumed more significance as a result of the diligent research which characterizes modern medicine. In this respect a recent study by J. S. Horner of varicocele among schoolchildren[1] has revealed an unsuspected frequency of the condition after puberty and has aroused some speculation on its aetiology and functional effect. In a painstaking review of over 1,200 boys, of whom the majority were aged between 11 and 16, a striking rise in the incidence of the condition was seen to occur at puberty, reaching a maximum of 21.5% at the age of 14½. Thereafter the incidence slightly declined, and in a group aged 17 to 32 the figure dropped to about 15%. The somewhat surprising incidence revealed by this review naturally prompts inquiry into the diagnostic criteria employed, but these are fully described and would appear unimpeachable. Three groups of varicocele were defined, depending on the digital recognition of elongation, dilatation, and tortuosity of the pampiniform plexus accompanied by a cough impulse (mild), manual and visual evidence of the classical "bag of worms" (moderate), and massive tortuosity of the veins which impeded clinical examination of the testicle (marked). Of the 193 varicoceles detected, 63 were regarded as being mild, 87 moderate, and 43 marked. All save one were on the left side and only 4 were recorded in pre-pubertal boys. To explain this Horner suggests that the venous return along the left testicular vein is possibly impaired in susceptible individuals and that this disability may become accentuated at puberty when the vascularity of the testicle increases. Such an effect may also be related to growth changes, particularly to gain in height and weight over this period, but though the report is amply comprehensive in these respects no statistically significant conclusions can be drawn.

In a few cases spontaneous improvement occurs with time, and this no doubt accounts for the slightly lower incidence in adults, but nevertheless the overall frequency given for them too remains remarkably high.

As to the functional significance of varicocele, much has been written in recent years on its relationship to subfertility.[2] Such an association has become widely recognized because many authors have reported low sperm counts in association with varicocele in adults, and improvement in the sperm counts after surgical treatment of the condition.[3,4] Even the proportion of men with varicocele attending a subfertility clinic has been adversely compared with the small number of similar men accompanying their wives to an antenatal department.[5] Nevertheless it remains difficult to explain the mechanism of subfertility purely on the basis of a predominantly unilateral vascular defect, and it may still be doubted whether the latter may not play a secondary role in association with underlying gonadal deficiency. However, the article by Mr. L. Stuart Scott appearing in the *Journal* this week at p. 788 gives detailed evidence of improved fertility, as shown by an increased sperm count and pregnancy rate, after surgical treatment. Emphasizing again the importance of clinical grading, he suggests that the size of the varicocele has a direct influence on the degree of subfertility. This is supported by convincing evidence of improvement in the sperm counts of 88 men who were operated on for major lesions. In this series preoperative investigation of the seminal fluid showed gross impairment in a majority (including six cases of azoospermia), and the cases were grouped according to the size of the sperm count. After operation a distinct improvement occurred throughout the series, with positive results in three of the previously azoospermatic cases.

The consistency of such improvement throughout each group is particularly impressive and leaves little ground for doubting the adverse effect of varicocele, at least in its grosser forms, on fertility. Nevertheless, in view of the high incidence of the condition reported in schoolchildren, its potentialities in this respect are probably not so serious as they might at first appear.

[1] Horner, J. S., *Med. Offr.*, 1960, **104**, 377.
[2] Harrison, R. G., *Brit. med. J.*, 1954, **2**, 300.
[3] Tulloch, W. S., *Edinb. med. J.*, 1952, **59**, 29.
[4] —— *Brit. med. J.*, 1955, **2**, 356.
[5] Russell, J. K., *Ibid.*, 1954, **1**, 1231.

MÉNIÈRE'S DISEASE

Since his original paper exactly one hundred years ago,[1] the triad of vertigo, tinnitus, and deafness has been called Ménière's disease or Ménière's syndrome. Ménière was chiefly concerned to distinguish a series of symptoms which had hitherto been considered due to cerebral vascular disease. Pointing out that even after dramatically sudden falls into unconsciousness the patient suffered no residual disability on recovery, unlike in true cases of cerebral catastrophe, he laid great stress upon the fact that the patient was later handicapped only by a gradual and progressive loss of hearing, which might ultimately become total deafness. He cited Flourens's experiments with birds to explain why he believed that the vertiginous symptoms experienced by the patients he had observed might be due to a lesion of the labyrinth. Apparently only one opportunity offered of testing his inference, and this was not in a particularly typical case. He described a girl who experienced vestibular symptoms while riding outside on a stage coach and shortly afterwards died. At necropsy he found a reddish exudate in the membranous labyrinth. This case would hardly qualify as an example of Ménière's disease as we are now accustomed to think of it. C. S. Hallpike and H. Cairns[2] were able to examine histologically the labyrinths of two patients suffering from Ménière's disease who died shortly after operations for division of the eighth nerve. The most important finding was a grossly distended cochlea duct, degeneration of the organ of Corti, and atrophic changes in the stria vascularis. The occurrence of these changes has been confirmed in several cases of Ménière's disease, but not in others. These changes in the cochlea apparatus hardly explain symptoms referable to the vestibular part of the inner ear, and an entirely convincing pathological lesion in the semicircular canals has yet to be recorded.

The phasic nature of the attacks and the physical well-being of the patient between them have led to the suggestion that the symptom was due to vasospasm in the blood vessels of the end organ. The late James Seymour summarized some of his work on this aspect of the problem in a paper[3] published shortly before his recent tragic death, describing how the conception of vasomotor instability had been fructifying since M. Lermoyez[4] postulated spasm in the internal auditory artery. He demonstrated alterations in calibre of the capillaries in the spiral ligament (presumably in the cat), and in one experiment the local application of a weak solution of adrenaline was noticed to cause spasm in a terminal arteriole for many hours. Before these findings can be accepted as explanations of, or even as running parallel with, the abnormalities in man which lead to Ménière's triad, they must await confirmation by other workers and the establishment of a closer relationship between these animal experiments and human physiology and pathology. Nevertheless, cervical sympathectomy has been performed in cases of Ménière's disease, and improvement reported in the hearing as well as in the attacks of vertigo.[5] The operation, based on the patient's response to previous stellate-ganglion block and on the validity of Seymour's experiments, is supposed to abolish vacoconstrictor innervation in the labyrinth. But others who have tried the method have not obtained uniformly successful results.

Ménière noticed, and it is now unquestionably accepted, that one or other of the triad of symptoms could appear many years before the others, and that there were often long intervals of remission between the attacks of vertigo. At different stages of the disease diagnosis may therefore be difficult. In the final assessment of a case, uncertain factors may be introduced, for the recorded incidence of Ménière's disease varies a great deal. The number of cases reported from a large neurological clinic,[6] a large general hospital,[7] both in the London area, and from Northern Ireland[8] and Kent,[9] differ widely. In every case, even in the apparently obvious ones, careful neurological and otological examination is essential. An audiometric reading of the patient's hearing must be done, and the conditions under which this is performed should be standardized. The deafness present must be of the perceptive type, and recruitment (the gradual increase in reaction to a stimulus of the same intensity) should also be demonstrable—difficult in some cases without an audiometer of the Békésy type. The function of the labyrinth can be tested by the controlled rotation of the patient in a special chair or by stimulation of the semicircular canals with hot and cold water syringed into the external auditory meatus. The accuracy of these tests is improved by electrical means of recording the nystagmus. Caloric stimulation tests each labyrinth separately and is easily performed in clinical practice. The external semicircular canal is the one

[1] Ménière, P., *Gaz. méd., Paris*, 1861, **16**, 29, 88, 379, 597.
[2] Hallpike, C. S., and Cairns, H., *Proc. roy. Soc. Med.*, 1938, **31**, 1317.
[3] Seymour, J. C., *J. Laryng.*, 1960, **74**, 599.
[4] Lermoyez, M., *Presse méd.*, 1919, **27**, 1.
[5] Golding-Wood, P. H., *J. Laryng.*, 1960, **74**, 803.
[6] Cawthorne, T., ibid., 1956, **70**, 721.
[7] Ellis, M., ibid., 1956, **70**, 721.
[8] Wilmot, T. J., ibid., 1956, **70**, 725.
[9] Williams, D., *Trans. med. Soc. Lond.*, 1957, **74**, 15.
[10] Dandy, W. E., *Surg. Gynec. Obstet.*, 1941, **72**, 421.
[11] Portmann, G., *Arch. Otolaryng. (Chicago)*, 1927, **6**, 309.
[12] Krejci, F., and Bornschein, H., *Arch. Ital. Otol.*, 1951, **62**, 1.
[13] Arslan, M., *Minerva otorinolaryng. (Torino)*, 1953, **3**, 141.
[14] James J., Angell, Dalton, G. A., Bullen, M. A., Freundlich, H. F., and Hopkins, J. C., *J. Laryng.*, 1960, **74**, 730.

usually tested, and gross impairment of function, or canal paresis, is the usual finding.

It is only in recent years that the performance of these tests has become routine in otological clinics outside large centres, and the possibility of obtaining these reasonably accurate objective measurements of otherwise very indefinite subjective symptoms has greatly improved clinical diagnosis. Furthermore, cerebral arteriography has helped in the diagnosis of certain types of cerebral arterial disease. As a result, the symptom of vertigo is being more accurately assigned to causes. In the past few years some cases which might previously have been called cases of Ménière's disease have been shown to be due almost certainly to disease in the vertebral arteries and to insufficiency in the basilar artery.[9] Many more cases are being placed in the category of benign positional vertigo: in fact, this condition is now almost the most common reason for the symptom. It closely resembles Ménière's disease in some of its aspects, but it rarely affects the hearing, while labyrinth function tests are usually normal.

So far as treatment of Ménière's disease is concerned, most cases respond to encouragement, management, and sedation, if earnestly applied with all the resources of the art of medicine.[7] Other medical measures, including salt-free diets and restricted fluid intake, the exhibition of histamine or nicotinic acid, or both, and, in bilateral cases, streptomycin, have been employed with success. However, there are cases which resist medical treatment. Surgical treatment has been directed to division of the vestibular portion of the eighth nerve in the posterior fossa,[10] a logical method of approach, since it preserves the residual hearing. Drainage of the endolymphatic sac has been advocated.[11] Both methods are relatively unfashionable in modern practice. Usually the hearing in Ménière's disease gradually deteriorates, and it has often been observed that when the hearing becomes extremely poor the attacks disappear: that is to say, when the labyrinth dies, no further upsetting reactions are initiated from it. During its slow death, the functions of the opposing labyrinth gradually compensate for its loss. It follows that in unilateral cases destroying the labyrinth, by injecting it with alcohol or by other means, can stop the attacks. However, the disease is bilateral in a percentage of cases, varying from 5 to 30 and probably depending upon the length of time they are under observation. Therefore some method, which is simpler, safer, and more certain than intracranial division of the vestibular nerve, has been sought of destroying the vestibular function while preserving that of the cochlea.

Destruction of the labyrinthine part of the inner ear by ultrasonic vibrations has been introduced,[12 13] and a group of workers in Bristol[14] have recently surveyed some of the difficulties they encountered with this method. They describe the various effects of ultrasonic radiation on living tissue, and there is no doubt that the action of the rays can be lethal.

The technique of the method is to deliver a lethal dose of ultrasonic radiation to the labyrinth by placing the applicator firmly against the bony wall of the external semicircular canal after exposure by a mastoid operation. Transmission of ultrasound is poor in bone, and even worse in air. Fluid is the medium in which it prefers to travel, and faulty positioning of the applicator from which the rays are emitted, or fluid in contact with it, may lead to diffusion of harmful radiation to the facial nerve, the cochlea, the temporo-sphenoidal lobe, and the cerebellum. Moreover, the amount of radiation being given is hard to measure and to focus. The Bristol team give a clear account of how they have surmounted some of these difficulties and how they are in the process of overcoming others. At present, the effect of the rays is determined by watching the patient's nystagmus, and from previous experience obtained with the procedure.[13] Such rule-of-thumb checks are unsatisfactory, but the difficulties are probably not insuperable. It has already been found that one application may often cause complete degeneration of the labyrinth without involving the cochlea or other organs. In some cases a second application has been necessary. Expensive equipment and the services of trained physicists are essential, but with increasing experience the method may be very useful in the treatment of the difficult bilateral cases. Mr. J. Angell James gave an encouraging report of the results of the Bristol team at the recent Annual Meeting of the B.M.A. in New Zealand (see last week's *Journal*, p. 736), but until the technique becomes really foolproof, ultrasound should probably not be employed in unilateral or uncomplicated cases.

THE FLEMING MEMORIAL

The name of Sir Alexander Fleming, who died six years ago, is to be commemorated in the way which would have pleased him most and which is especially fitting for one whose research has brought such immense benefits to mankind. On March 16, in the

Guildhall of the City of London, a great project was announced—the setting up of the Fleming Memorial Fund for Medical Research,[1] with a target of raising forthwith in Britain an initial endowment of £1m.

The Fund was launched under impressively favourable auspices. For its patron the Fund has the Queen Mother, for its president Lord Birkett, for its chairman of trustees Lord Heyworth, and for its chairman of council Lord Tenby. Three distinguished scientists—Sir Lindor Brown, Sir Hans Krebs, and Professor P. B. Medawar—are among the seven trustees, and there is a small scientific advisory committee under the chairmanship of Sir Harold Dodds. On the council of the Fund are representatives of medical organizations, of universities, of science, of the law and other professions, of industry, and of finance—and among the individual members are Lady Fleming, Sir Alexander's widow, and Dr. Robert Fleming, his son. Among the vice-patrons and vice-presidents are the Prime Minister, the Archbishop of Canterbury, and Sir Howard Florey, P.R.S., who with Professor E. B. Chain brought the promise of Fleming's original discovery to fulfilment. That all these people are actively concerned in the establishment of the Fund is in itself a moving tribute to the memory of Sir Alexander Fleming.

In an obituary tribute to Sir Alexander Fleming, Sir Henry Dale wrote in this journal: "The world has surely made no mistake in regarding the discovery of penicillin, and its introduction into therapeutics, as providing one of the outstanding landmarks in the progress of medical science." In commemorating the great achievement the organizers of the Fund are right to expect a matching generosity from the public in Great Britain and overseas. As Lord Birkett writes in his presidential message, "The Memorial Fund contemplates assistance to research on a great scale, and it will need money on a great scale too." It is now up to Britain and the world—the appeal is an international one—to provide the Fund with money that will enable it to achieve its admirable aim of advancing and expanding "basic medical research designed to elucidate the causes of disease and assist in its prevention and cure." These are objects which the medical profession can wholeheartedly support.

Some may ask why there is a need to subsidize medical research by voluntary donations in a country where there is a National Health Service and Government agencies to undertake and pay for research. The answer is in the first place that nowhere near enough money is spent on basic medical research. Secondly, although the work of the official bodies is of the very highest quality, and their often meagre financial grants are spent to the best advantage, independent funds and foundations have more freedom of action. They can often make grants to gifted individual scientists more quickly and can provide expensive apparatus more readily. They can support medical research in universities whose funds cannot stretch beyond their educational commitments, and they can hasten the adoption of new approaches in scientific investigation. There are not enough able men and women to-day doing basic medical research work, with freedom to pursue their own lines of inquiry, nor are there funds available to support any large addition to their ranks. And there are medical research institutions in real need of help. The Fund has two such institutions especially in mind—the Wright-Fleming Institute of Microbiology at St. Mary's Hospital and the Sir William Dunn School of Pathology at Oxford, both closely concerned with the original work on penicillin.

If the response to the appeal comes up to expectations the Fund will be in a position to provide for research institutions the practical assistance they need and for individuals of outstanding ability the working environment in which they can develop their talents for research to the greatest advantage. And Fleming's name will be for ever linked with these benefactions.

[1]The Fleming Memorial Fund for Medical Research, 26 Upper Brook Street, London W.1.

CYSTICERCOSIS

The adult stage of the tapeworm *Taenia solium* is an intestinal parasite of man. The larval stage generally parasitizes swine, causing "measly pork," but occasionally it too may infest man, causing the disease known as cysticercosis. The cysticerci lodge in striated muscle and in the central nervous system. They are usually symptomless in the muscles, where they calcify readily. In the brain they may form small isolated cysts in the meninges or the parenchyma of the brain; they may form large thin-walled mobile racemose cysts in the ventricles or basal cisterns; or they may cause an intense arachnoiditis. Most of our knowledge of the disease in this country stems from the pioneer work of Sir William MacArthur[1,2] and H. B. F. Dixon,[3,4] who established its importance as a cause of epilepsy in troops who had served in India, while its incidence among refugees from Eastern Europe was later stressed by E. R. Bickerstaff.[5]

H. B. F. Dixon and F. M. Lipscomb[6] have now completed a detailed analysis and follow-up of 450 British cases, 98% of whom had contracted the disease

[1] MacArthur, W. P., *Trans. roy. Soc. trop. Med. Hyg.*, 1933, **26**, 525.
[2] —— ibid., 1934, **27**, 343.
[3] Dixon, H. B. F., and Smithers, D. W., *Quart. J. Med.*, 1934, **3**, 603.
[4] —— and Hargreaves, W. H., ibid., 1944, **13**, 107.
[5] Bickerstaff, E. R., *Brit. med. J.*, 1955, **1**, 1055.
[6] Dixon, H. B. F., and Lipscomb, F. M., *M.R.C. Report on Cysticercosis: An Analysis and Follow-up of 450 Cases*, 1961. H.M.S.O., London.
[7] Bickerstaff, E. R., Small, J. M., and Woolf, A. L., *Brain*, 1956, **79**, 622.
[8] —— Cloake, P. C. P., Hughes, B., and Smith, W. T., ibid., 1952, **75**, 1.

in India. A history of intestinal taeniasis was eight times higher in these cases than in other troops; 92% had epilepsy as the main symptom and 54% subcutaneous (intramuscular) nodules. Other symptoms were much less frequent in this series, mental changes occurring in only 8.7% (appreciably less than previously thought), intracranial hypertension in 6%, and focal cerebral lesions in 3%, while 3% were entirely free of symptoms. Though intervals from exposure to first symptoms of up to 30 years were recorded, there was a five-to-one chance of symptoms developing within seven years. The diagnosis was made by biopsy of a subcutaneous nodule in 25% and by the radiographic demonstration of calcified cysts in 75%, stress being laid on the importance of *x*-raying the muscles, as opposed to the skull, where calcification is less complete, often inconspicuous, and occurs later. In fact there was only one case in which calcification was present in the skull alone. Immunological tests were of little value, and eosinophilia was very variable; this may be intense though transient in exacerbations of the disease.[7] The long-term prognosis was found to be better than might be thought, and only 42 of the 450 had died, many remaining free of symptoms for many years. Treatment is essentially that of the epilepsy, and attempts at removal of cortical cysts are of little value.

Bickerstaff and his colleagues[7 8] have described how the intraventricular racemose cysts cause symptoms of intermittent obstructive hydrocephalus, together with recurrent attacks of meningo-encephalitis during which the cerebrospinal fluid contains abundant lymphocytes and gives a paretic Lange curve. Changes in the blood vessels may cause sudden cerebral infarction or gradual cerebral atrophy. Interference with the racemose cysts causes an intense allergic meningeal reaction, which may be fatal. Administration of cortisone is desirable for any operative procedure and it is wiser to limit surgery to relief of the obstruction.

It is over thirteen years since British troops last served in India and cysticercosis is a dying disease in Western Europe, but its incidence is still high in Eastern Europe and in Central and South America. As world travel increases new cases may still appear from time to time in Great Britain. It is also important to remember that human cysticercosis is not caused by eating measly pork, but by the ingestion of tapeworm ova, so that a food-handler harbouring a tapeworm may infest many people who have never visited an area where the disease is endemic.

MICTURITION SYNCOPE

Sudden changes in distribution of blood are monitored by baroceptors located in the heart and great vessels. These tend to restore homoeostasis by means of reflex mechanisms which adjust either the stroke output of the heart or the peripheral circulation or both. Much insight into baroceptor responses has been provided by the careful researches of E. P. Sharpey-Schafer and his colleagues during the last few years.[1] If compensation fails or cannot be achieved because of additional burdens on the baroceptor mechanism, syncope may result. Circulatory adjustments are complex, but a simple illustration is provided by considering the effects of posture. On assuming the upright position a temporary fall in the pressure of blood going to the heart, and hence in stroke output, is compensated by peripheral vasoconstriction. In some subjects especially the elderly and debilitated, vasoconstriction may be delayed, with a consequent sensation of faintness. Factors which favour vasodilatation, such as heat and hypotensive drugs, increase the tendency to syncope, particularly if accompanied by prolonged immobility as in the soldier on the parade ground. Dangerous situations may arise if the upright position is forcibly maintained, as in crowds, pilots strapped into the seat of jet aircraft, and patients undergoing dental anaesthesia.[2 3] As every first-aider knows, the correct treatment for syncope is to lay the patient flat.

Additional factors which strain baroceptor mechanisms are hyperventilation, coughing, and performance of the Valsalva manœuvre,[4] not only by causing peripheral vasodilatation but also by increasing intrathoracic pressure and thus reducing stroke output. A familiar clinical example is cough syncope, in which a prolonged bout of coughing in an emphysematous and often obese patient suddenly ends in loss of consciousness. Less well known, though probably commoner than is generally thought, is micturition syncope, several examples of which have recently been described.[5 6] The condition has all the elements of other varieties of syncope. The subject, invariably a healthy male, wakes in the night with a full bladder and a desire to micturate. The warm bed and perhaps recent consumption of alcohol makes for peripheral vasodilatation. The act of straining—performing a Valsalva manœuvre—raises intrathoracic pressure, and consciousness is lost. A recent case report[6] suggests that functional obstruction of the bladder neck may be responsible for the syncopal attacks, and the patient was cured by a plastic operation on the bladder. Such examples of syncope—and there are others—are not merely academic demonstrations of circulatory physiology. An understanding of baroceptor mechanisms and a careful history will provide the clinician with the means of reassuring the patient and in most cases of preventing further attacks.

UNUSUAL INFLAMMATORY REACTIONS OF THE EYE

Until fairly recently syphilis, tuberculosis, and focal sepsis were the three aetiological factors generally invoked to explain inflammatory reactions of the choroid and of the retina. The recognition some twenty years ago of toxoplasmosis as a cause of congenital

[1] Sharpey-Schafer, E. P., *Brit. med. J.*, 1956, **1**, 506.
[2] Bourne, J. G., *Lancet*, 1957, **2**, 499.
[3] Sharpey-Schafer, E. P., Hayter, C. J., and Barlow, E. D., *Brit. med. J.*, 1958, **2**, 878.
[4] Howard, P., Leathart, G. L., Dornhorst, A. C., and Sharpey-Schafer, E. P., ibid., 1951, **2**, 382.
[5] Proudfit, W. L., and Forteza, M. E., *New Engl. J. Med.*, 1959, **260**, 328.
[6] Eberhart, C., and Morgan, J. W., *J. Amer. med. Ass.*, 1960, **174**, 2076.

lesions in the fundus was followed by the incrimination of rubella as a further cause of such defects, not only of the retina and choroid but of the eye as a whole. Recognition of other than the classical causes of chorio-retinal inflammation for acquired lesions in adults has a more recent history. Studying eyes excised from adult patients, Helen Wilder[1] detected organisms resembling toxoplasma in inflammatory chorio-retinal lesions. Subsequently toxoplasma came to be isolated from the eyes of patients with recurrent chorio-retinitis, but it is largely on serological studies that toxoplasmosis is now established as a well-defined clinical group; how common it is, is still not clear. Recently attention has been drawn in these columns to another cause of chorio-retinal inflammation—cytomegalic inclusion disease in infants.[2 3] Now two further developments need to be noted—histoplasmosis and *Toxocara* infection.

A. C. Woods and H. E. Wahlen,[4] in a comprehensive survey on histoplasmosis, recall that this fungus infection, which was once regarded as a fatal disease in man, appears normally to run a mild subclinical course and is widespread as an unsuspected and asymptomatic infection in certain areas. It has been claimed that there are 20,000,000 cases of the subclinical disease in the United States. Like tuberculosis, the clinical course of which it resembles to some extent, it produces an allergic state. The infection can be suspected when a histoplasmin sensitivity test is positive and there is pulmonary calcification with a negative tuberculin test. In 19 out of 62 patients with granulomatous uveitis, they found a peculiar and consistent pattern: discrete, atrophic foci with little or no pigment were followed by a cystic lesion at or near the macula. About one-half of these central lesions showed a surrounding haemorrhagic reaction. In nine of these patients there was the triad of histoplasmin sensitivity, pulmonary calcification, and anergy to tuberculin. In the other ten the evidence for a benign systemic histoplasmosis was not so clear cut.

Two years before her work on toxoplasmosis Helen Wilder[5] established *Toxocara* as an infection of the retina when she showed nematode parasites in the retina of a large number of eyes removed for pseudoglioma. In 1956 R. L. Nichols,[6] working with Wilder's material, recognized the nematode as the second-stage larva of *Toxocara canis*. Confirmatory work has come from W. C. Irvine and A. R. Irvine[7] from California, and from N. Ashton[8] in London. Ashton gives a full report of four eyes excised from children. In these cases *Toxocara* could be isolated from a solitary retinal mass in the central area of the fundus.

Such information as is available on *Toxocara* infection shows it to be common in dogs throughout the world, including Great Britain. The general manifestations in man have been recognized only in recent years, and it is clear now that ocular involvement must be regarded as one of the forms of human *Toxocara*. How frequent human infection is and how important this parasite is in causing pseudoglioma of the retina remain to be established. Eosinophilia might give a useful lead in suspected cases.

[1] Wilder, H. C., *Arch. Ophthal.* (*Chicago*), 1952, **48**, 127.
[2] *Brit. med. J.*, 1959, **2**, 558.
[3] Ibid., 1960, **1**, 1947.
[4] Woods, A. C., and Wahlen, H. E., *Amer. J. Ophthal.*, 1960, **49**, 205.
[5] Wilder, H. C., *Trans. Amer. Acad. Ophthal. Otolaryng.*, 1950, **55**, 99.
[6] Nichols, R. L., *J. Parasit.*, 1956, **42**, 349.
[7] Irvine, W. C., and Irvine, A. R., *Amer. J. Ophthal.*, 1959, **47**, 185.
[8] Ashton, N., *Brit. J. Ophthal.*, 1960, **44**, 129.

MAMMARY SOUFFLE

Patients in middle and late pregnancy are often referred to cardiologists for further elucidation of cardiac murmurs. It is usual for there to be ejection systolic murmurs which are heard over the pulmonary artery and which are accentuations of similar murmurs heard in normal subjects. However, their loudness may be suggestive of pulmonary stenosis. Aortic systolic ejection murmurs are also frequently heard in pregnancy in the third and fourth left intercostal spaces close to the sternum. If any of these murmurs are accompanied by diastolic murmurs, or continue into diastole, other possibilities arise, such as aortic or mitral valve disease, patent ductus arteriosus, or venous hums.

The so-called mammary souffle of pregnancy and lactation must be added to the differential diagnosis. J. T. Scott and E. A. Murphy[1] reported two cases in which this simulated patent ductus arteriosus. More recently B. Tabatznik and colleagues[2] examined 257 women in pregnancy and the puerperium and found a mammary souffle in 15.3% in the post-partum period, 13.3% in the third trimester of pregnancy, and 17.9% in the second trimester. It was not heard in the first trimester. The murmur was most often heard in the second intercostal spaces, but also occurred in the third and fourth left intercostal spaces. There was always an interval between the first heart sound and the onset of the murmur; it was sometimes heard only in systole, but at times continued into or throughout diastole. It was of high frequency and best heard with the patient lying flat. These authors suggest that during pregnancy and lactation blood may be preferentially diverted towards the breasts along the perforating branches of the mammary artery and that smaller amounts of blood may flow along the anterior intercostal branches of the internal mammary artery. This situation could result in such murmurs being produced at the sites of anastomoses between these vessels. If that were so it would account for the localization of the murmurs, their poor radiation, and their elimination by lateral compression in the corresponding intercostal space. It could also account for prominent intercostal pulsation near the site of the murmurs. These are interesting suggestions and might explain the fact that, when such murmurs disappear after suppression of lactation by stilboestrol, the local change in haemodynamics returns to normal. Whatever the explanation of the mammary souffle may be, its importance lies in the recognition of it and the frequency with which it occurs.

[1] Scott, J. T., and Murphy, E. A., *Circulation*, 1958, **18**, 1038.
[2] Tabatznik, B., Randall, T. W., and Hersch, C., ibid., 1960, **22**, 1069.

THE WORK OF A NURSE EMPLOYED IN A GENERAL PRACTICE

BY

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While everyone agrees about the importance of co-operation between doctor and nurse in the provision of an effective domiciliary medical service, the general administrative organization does little to ensure or encourage integration. Problems of co-ordination are accentuated by the tripartite division of the National Health Service, so that the extent to which integration is achieved depends largely on the individuals concerned.

Various local authorities and individuals have approached this problem in different ways. References are often made in nursing journals and reports of medical officers of health to schemes which are designed to bring the general practitioner and the public-health nurse into a working partnership, but we have remarkably little factual information about the nature of the work done by the doctor and the nurse under these different schemes.

One form of collaboration which is still comparatively rare in this country is for a nurse to work directly with a general practitioner. This paper describes the system adopted in two general practices in each of which a nurse was employed with two doctors and a medical social worker in a "family-doctor team." The organization of the nurse's work in this situation is described, and an analysis is given of the nature of the work which she performed and the type of illness with which she was most frequently concerned. Attention is focused on the nursing component of the routine work of the family doctor, and some practical problems of defining the roles of the doctor and nurse in this situation are revealed. The relationship of the nurses in these practices to health visitors and district nurses employed by the local health authority is discussed. Finally, the advantages and disadvantages of the wide-scale application of such an arrangement are considered.

Practices, Staff, and Patients

The two practices involved in this study together constitute the Edinburgh University General Practice Teaching Unit. Each practice is staffed by two doctors, a medical social worker, and a nurse. All the staff hold university appointments. Both nurses have additional qualifications and experience in midwifery, and one of them has been trained as a health visitor.

The size of the lists is relatively small, each practice having approximately 2,500 registered National Health Service patients, but all the staff have considerable teaching commitments. Every year approximately 150 medical students are attached to the unit for a period of three months for practical instruction.

*Now at the Institute of Community Studies, Bethnal Green, London.

The two practices are situated within half a mile of each other near the centre of the city. In this area there is a lot of old property, and housing conditions of the patients are much lower than the average for Scotland or Edinburgh. A considerable proportion of them live in overcrowded conditions, and the absence of such amenities as a bath and the exclusive use of a lavatory is not infrequent. A high proportion of the adult male patients are labourers and unskilled workers, and there are relatively few non-manual workers. In addition, the age distribution of the practice differs from that in Scotland or Edinburgh, there being an excess of children under 5 and a dearth of middle-aged people of 45–64 (Scott, Anderson, and Cartwright, 1960).

Material

During the twelve months October, 1956, to September, 1957, the doctors, almoners, and nurses in the unit recorded details of all their consultations on standard record sheets. The nurse's records provided information about the circumstances of the consultation, the diagnosis made by the doctor, and the examination and treatment carried out by her. All of this, apart from the diagnosis, was pre-classified so that she knew precisely the amount of detail required and the alternative classifications available. The classifications had been made after various pilot studies and discussions with the individuals involved. Social data about the patients and their families were recorded in a separate file.

Organization of Practices

Each practice has a waiting-room, two consulting-rooms for the doctors, a small consulting-room for the almoner, and a larger consulting-room, measuring approximately 20 by 15 ft. (6 by 4.5 m.), for the nurse. This is an all-purpose room which is equipped as a combined treatment and examination room, adjoining the doctors' consulting-rooms. In one practice an electric hot-air oven is used to dry-sterilize syringes: these are packed in aluminium screw-capped tubes for use in both practices.

Three "surgeries" (consulting hours) are held at each practice on week-days: 9–10 a.m., 3–3.30 p.m., and 6–7 p.m. The nurse is available for all morning and afternoon surgeries and for one evening surgery each week. In addition, both practices hold an ante-natal clinic once a week, where registered expectant mothers are seen by appointment, and in one practice a child-welfare clinic for the patients is held on one afternoon a week.

In the unit's earlier days the nurses undertook a considerable amount of home visiting, and at the time of the study (four years ago) they were still accepting some responsibility for the care of patients in their homes, although the doctors normally used the domiciliary services provided by the local health authority. In both practices effective collaboration with the local authority health visiting and district nursing service has been established, with the result that it is now quite exceptional for the practice nurse to do home visiting.

Other duties of the nurse include the supervision of surgery equipment and the contents of the doctors' bags. She attends a daily case conference at which she, the doctors, and the almoner report on their contacts

with patients during the preceding 24 hours, discuss their problems, and exchange information.

Finally, the nurse is largely responsible for maintaining and developing contacts with the local health authority services, and she arranges conferences between health visitors, district nurses, and the staff of the practice.

Number and Nature of Consultations with Nurse

At one practice the nurse was concerned in just over 3,000 consultations† in the course of the study year, and at the other practice the number was just under 4,000—a rate of between 12 and 16 consultations per working day for each nurse, and an average of about one and a half consultations per year for each registered patient.

The numbers and proportions of consultations at the normal surgeries, in patients' homes, and at the antenatal and child-welfare sessions are as follows:

At the normal surgeries	5,026	70·6%
In patients' homes	411	5·8%
Antenatal sessions	814	11·4%
Child-welfare ,,	867	12·2%
	7,118	100%

A quarter of the nurse's consultations were concerned with antenatal or child-welfare sessions and 6% took place in the patient's home.

Doctor and Nurse

How did the doctor and the nurse work together in practice? In what proportion of her consultations was the nurse seeing the patient on her own, and in what proportion was she working directly with the doctor? Who was mainly responsible for initiating consultations with the nurse, and when both the doctor and the nurse were involved in a consultation how did this arise?

At antenatal and child-welfare sessions both the doctor and the nurse were present as a matter of routine, and all patients attending would almost invariably see both of them. At normal surgery times the position was quite different, both doctor and nurse being available for consultation in their different rooms.

Patients consulting at the practice for the first time always saw the doctor. He might ask for the nurse's assistance during the consultation, he might send the patient in to see the nurse without also seeing her himself, or he might tell the patient to return for treatment to the nurse in a few days' time. Once the nurse had seen the patient she might make fresh appointments for the patient to see her or the doctor, and she would sometimes call the doctor in during the course of consultation. Sometimes, too, once a patient had consulted the nurse for one ailment he might go direct to her for another condition, but in such a case she would almost always consult the doctor. How often did these various contingencies arise in practice?

The doctors saw four times as many patients as the nurses at normal surgery hours, the ratio of doctor to nurse consultations being slightly under three to one at the morning and afternoon consulting hours when the nurse was nearly always available, and thirty to one in the evenings, when she was there only occasionally.

At two-fifths of the nurse's consultations the doctor was also present. On these occasions they conferred or worked together. This collaboration was more often initiated by the doctor than by the nurse:

		Percentage of Nurse's Surgery Consultations
Doctor involved	At his initiative	22
	At nurse's ,,	17
	By chance	1
Doctor not involved		60
Total No. of consultations (=100%)		5,026

Looking at this from the doctor's standpoint, we find that the nurse was involved in approximately one in ten of his surgery consultations, and this proportion varied between 13% at morning and afternoon surgeries and 2% in the evenings.

Sometimes the nurse accompanied the doctor on visits to the patient's home. During the study year this occurred on 51 occasions, which represent 12% of all the nurse's visits to patients' homes but only less than 1% of the doctor's visits.

How did the patients come to see the nurse during normal surgery hours? This information is given in Table I.

TABLE I.—*Methods by Which Patients Reached Nurse for Normal Surgery Consultations*

Method	Percentage of Consultations	Percentage of Consultations at which Doctor was Involved	No. of Consultations
From consultation with doctor	24	94	1,214
By appointment:			
Made by doctor	10	19	475
,, ,, nurse	55	22	2,763
Direct—patient's initiative	11	32	574
All consultations	100	40	5,026

The commonest type of attendance was the follow-up consultation when an appointment had been made at a previous consultation with the nurse. (The term "appointment" is used here loosely to indicate that it had been arranged previously that the patient should come to see the nurse, although a particular time and date may not have been arranged.) The patient went direct to see the nurse without any previous arrangement or referral by the doctor in about one in ten of her consultations.

The proportion of these different types of consultation in which the doctor was directly involved is shown in Table I. The proportion was greatest for those arising direct from a consultation with the doctor. In these cases it was, of course, the doctor who initiated the collaboration, but at the other types of consultation it was the nurse who had to decide whether or not the doctor should also take part in the consultation. She asked the doctor to see the patient at a fifth of the consultations which had resulted from an appointment, and this proportion was practically the same whether the appointment had been made initially by the doctor or the nurse. When the patient came to see the nurse on his own initiative she referred him to the doctor in a third of the cases.

Action Taken by Nurse

It is convenient to consider the nature of the work undertaken by the nurse in three broad groups. In the first section the nurse's role in diagnosis is considered by analysing the contribution she made to the examination of the patient; secondly, the nature of the treatment carried out by the nurse is recorded; and, finally, the part played by the nurse in supplying advice, explanation, or discussion is examined.

†A consultation with the nurse was recorded every time she saw a patient in a professional capacity, whether or not a doctor also took part in the consultation.

Examination

The nurse helped in the clinical examination of the patient at 41% of her consultations (Table II). This was much more common at child-welfare and antenatal sessions, for which it was practically routine, than at normal surgery attendances, and it rarely occurred at her visits to the patients' homes.

The nurse weighed the baby at more than nine-tenths of the consultations at the child-welfare sessions and she weighed the patient, tested the urine, and assisted the doctor in his examination of the expectant mother at the great majority of consultations during the antenatal sessions. During the normal surgery attendances the nurse's main contribution consisted in helping the doctor in the physical examination of the patient.

TABLE II.—*Type of Examination Carried Out by Nurse*

	Normal Surgeries	Patients' Homes	Child Welfare	Antenatal	All Consultations
	%	%	%	%	%
Assisting at examination by doctor	15	5	7	95	23
Weighing	10	—	93	94	29
Testing (mainly urine)	2	1	—	93	12
Taking specimens (mainly for bacteriology)	2	1	—	2	2
Temperature, pulse, respiration	1	—	—	—	1
Other examination	—	—	—	—	—
No examination	74	94	5	3	59
No. of consultations (=100%)	5,026	411	867	814	7,118

Treatment

At three-fifths of all their consultations the nurses performed some type of action that had a direct therapeutic purpose: this occurred at 75% of nurse consultations during routine surgery hours, and was even more evident (82% of all consultations) when she visited the patients' homes. The figures were very much lower for child-welfare and antenatal sessions, being only 18% and 3% respectively of these consultations. The type of action performed is shown in Table III.

TABLE III.—*Type of Direct Therapeutic Action Performed by Nurse*

	Normal Surgeries	Patients' Homes	Child Welfare	All Consultations
	%	%	%	%
Dressings	42	50	17	35
Supervision of personal hygiene	7	20	1	7
Eye-drops, ointment	8	—	—	6
Therapeutic injections	13	16	—	10
Supporting bandages	4	1	—	3
Topical treatment of ear conditions	8	—	—	5
Fitting birth-control appliances	1	—	—	—
Administering medicines	1	—	—	—
Other therapeutic action	8	15	—	6
No direct therapeutic action	25	18	82	39
No. of consultations (=100%)	5,026	411	867	7,118*

* Consultations at antenatal sessions are included in the proportions for all consultations, but no separate figures are given, since only at 3% of these consultations was any direct therapeutic action taken.

By far the most frequent type of therapeutic action undertaken by the nurse was the application of dressings—for example, in the treatment of skin diseases, such as infantile eczema, or in the topical treatment of boils, infected wounds, and abrasions. Some form of dressing was applied at 35% of her consultations, at 42% of normal surgery consultations, and at 50% of those taking place in patients' homes.

The supervision of personal hygiene, which included any washing or bathing (apart from that done before applying a dressing), was also relatively frequently performed at home visits, and injections were also given quite often under those circumstances. The nurse gave an injection at 10% of her consultations, and a substantial amount of work was concerned with the supervision of topical treatment for eye and ear infections. Included under the heading "other therapeutic action" were such things as enemas, douches, throat paintings, and nose drops.

Advice, Discussion, Explanation, and Listening

Apart from her other direct therapeutic activities, the nurse gave advice and information to patients, and explained various aspects of their illnesses or various normal physiological functions. She also listened to their accounts of their doubts and dilemmas, fears and frustrations. This aspect of her work is analysed in Table IV.

TABLE IV.—*Advice, Discussion, Explanation, and "Therapeutic Listening" Provided by Nurse*

	Normal Surgeries	Patients' Homes	Child Welfare	Antenatal	All Consultations
	%	%	%	%	%
Advice, discussion on:					
Diet, nutrition	18	40	86	38	30
Health, normal physiology	15	16	74	69	28
Disease	24	34	9	6	21
Exercises	6	6	9	45	11
Personal relationship problems	4	1	2	6	4
Vaccination, immunization	1	—	12	—	2
Birth control	2	—	—	2	2
Sex—other than birth control	1	—	—	1	1
Self-prescribed medicines	—	1	—	—	—
Other topics	2	—	1	2	2
Therapeutic listening	21	50	13	23	22
No discussion, advice, or listening	32	—	1	1	23
No. of consultations (=100%)	5,026	411	867	814	7,118

Advice on diet included dietetics, nutrition, home economics, budgeting, and often detailed examination of the medical and social aspects of the nutritional problem presented not only by the patient but by the family concerned. One aspect or another of this topic was the subject of advice or discussion at three out of every ten of all the nurse's consultations. The proportion was highest at child-welfare sessions, but it was also a relatively frequent topic for discussion at antenatal sessions and at the nurse's home visits. The nurse described some particular physiological process at over a quarter of her consultations, and again this was most frequent at antenatal or child-welfare consultations, whereas an explanation about the nature of a disease often took place at a normal surgery consultation or at home visits. This latter type of explanation was not recorded if the nurse merely told the patient the diagnosis; it was reserved for occasions on which the nurse explained the cause of the illness, how it was likely to develop, how the signs and symptoms were connected, when she reassured the patient that he did not have some particular sinister condition, or when she cleared up a misconception about the course or consequences of his illness.

Exercises were most often discussed at antenatal sessions, and vaccination and immunization at the child-welfare consultations. Birth control was discussed at only 2% of her consultations, and sex, other than birth control, at 1%. Other types of personal relation-

ship were the subject of conversation at 4% of all the consultations.

The nurse, in addition, often helped the patient to express latent fears and fantasies. She received many confidences and listened to many stories of strife and tales of tribulation. "Therapeutic listening" was recorded when she felt that the patient had benefited—not because of anything she had done or said but because she had just let him talk. This form of therapy was recorded at one in five of all consultations and at as many as half the home visits. Not surprisingly, it was lowest at the child-welfare sessions, but even here the mother bringing her child to the nurse was afforded this form of treatment at 13% of attendances.

Further analysis* showed that the nurse's activities at normal surgery consultations varied in relation to the person initiating the consultation. The nurse was most likely to be involved in examination or other diagnostic procedures when the doctor initiated the consultation, whether directly or by appointment. The nurse carried out some form of treatment most frequently when she herself initiated the consultation, and the patient came to see her by appointment at her suggestion. The extent to which she provided advice, explanation, and information, or lent a sympathetic ear, did not vary much with the person initiating the consultation, but it was highest when appointments were made by the doctor. Clearly, the doctor used the nurse as an adviser, and consciously or otherwise passed on to her some patients who had a greater than average need for therapeutic listening.

Effect of the Nurse on the Doctor's Work

In this study it is not possible to examine the effect of the nurse on the nature and extent of the doctor's work. To do this would necessitate an analysis of his work before and after the introduction of the nurse into the family-doctor team. It is, however, possible to examine certain aspects of his work under different circumstances during the study year, and this will provide some indication of the way in which the availability of the nurse influenced the type of action undertaken by the doctor at different consultations.

Although the nurse was generally present at morning and afternoon surgeries there were occasions when, because of illness, holidays, or various commitments associated with her work, she was not available during these periods, and the variation in certain of the doctor's actions under those circumstances is examined in Table V. (The figures given are for all surgery attendances, but detailed analysis reveals the same trend if the nurse is not available, no matter whether this is a morning, afternoon, or evening surgery.)

TABLE V.—*Variation in Doctor's Action with Availability of Nurse*

	All Surgeries	
	Nurse Available	Nurse Not Available
Type of action:	%	%
Dressings	8·0	14·3
Ear syringe	0·2	0·3
Therapeutic injections	1·2	2·5
Type of examination:		
Patient undressed	40·7	36·1
Couch used	11·0	7·3
No. of consultations (=100%)	11,326	8,604

*Detailed statistical tables and analyses are available, on request, from the authors.

In general, the doctor tended to do fewer dressings, give fewer injections, and perform more extensive physical examinations when the nurse was available. This demonstrates again that the nurse undertakes certain therapeutic functions on her own, but in regard to examinations and diagnostic procedures her most frequent role is that of assisting the doctor.

Nurse and Almoner

A discussion of the work carried out by the nurses in these two practices would be incomplete without some reference to the relationship between the nurses and the medical social workers who, with the doctors, make up the family-doctor team.

Total consultations given during the study year (including those for temporary patients) by doctors, nurses, and almoners were 32,418, 7,118, and 2,715 respectively. This gives a ratio of 11.9:2.6:1. The doctor's consultations outnumbered those of the nurse by just over 4½ to 1; but the nurse, whose hours of duty were identical with those of the medical social worker, had 2.6 consultations for every one given by her almoner colleague. The almoner saw fewer patients and on average gave more time to the patient than did the nurse. In contradistinction to her method of working with the doctor, the nurse rarely saw the patient along with the almoner—liaison and integration being normally effected at the daily case conference. Apart from routine daily reports, the almoner referred the problem back to this case conference at 9% of her consultations, and at 1% of her consultations she sent the patient back to the nurse in the unit for specific advice or information. The almoners recorded that 4% of their consultations were initiated by the nurses, and a relatively high proportion of these referrals were maternity cases.

Different Types of Disease with which Nurse was Concerned

Compared with the doctor, the nurse was relatively more concerned with skin conditions, pregnancy, accidents and injuries, child welfare, diseases of eyes and ears, diseases of the female genital organs, varicose veins, and obesity.* All these represent a greater *proportion* of the nurse's than of the doctor's consultations, although for these conditions the *number* of consultations was greater for the doctor than for the nurse. Fairly common conditions which represent a higher proportion of *doctor's* than of *nurse's* consultations are cardiovascular degeneration, bronchitis, vague symptoms, coryza, sore throats, psychoneurosis, exanthemata, and dyspepsia.

The nurse was seen at some time or other for just under one in five of all episodes of illness. Conditions for which she was most likely to be consulted were pregnancy, child welfare, boils, diseases of the female genital organs, wax in ears, impetigo and acne, and cuts and grazes; and she was concerned in a third or more of such episodes. These conditions all demand either examination, at which the nurse can assist the doctor, or dressings, the most frequent type of direct therapeutic actions performed by the nurse.*

Conditions which led to high consultation rates *per patient consulting* were of a different nature, being mainly chronic or long-term conditions—malignant

*Detailed statistical tables and analyses are available, on request, from the authors.

disease, eczema, cardiovascular degeneration, varicose veins, pregnancy, pulmonary tuberculosis, psoriasis, asthma and other allergies, and rheumatic diseases. If a nurse was consulted at all for these conditions the patient was seen by her, on average, more than four times.*

Analysis of nurse/patient consultations by age and sex* suggests that the nurse would be consulted most often in practices with a high proportion of young children and women of child-bearing age.

Discussion

That there is a substantial nursing component in the daily work of the family doctor is well recognized, and a number of general practitioners, mainly those working in partnership, provide out of the practice income a person to assist them in this respect. Such auxiliaries are by no means always fully qualified nurses, and, though some of the tasks they perform may not require a high degree of skill or training, these auxiliaries presumably are employed because of existing gaps in the nursing service available to the general practitioner. Apart from any nursing assistance which is provided by hospital out-patient departments, the nursing services available to the general practitioner can be reinforced by a wide range of services provided in the community. District nurses, midwives, health visitors, and school nurses are employed by the local authority. Many factories provide an industrial nursing service, and there is still room for voluntary societies, religious orders, and private enterprise to make a contribution in this field. With few exceptions, however, none of these services is available at the consulting-room, where the general practitioner does most of his daily work. Most of these services have this in common, that the nurses are employed by an organization or an authority which determines the type and range of service which will be provided, the general practitioner having little influence on determining policy and no direct executive authority to control or modify in detail the day-to-day work of the nurse or nurses concerned.

When a general practitioner, therefore, is confronted with a situation where he has complete access to the services of a fully trained nurse to assist him in the work of his practice, there is no substantial recorded experience to guide him to the most effective way in which they can work together as colleagues. His approach to this problem is therefore likely to be largely empirical and to be continued by preconceived ideas, partly derived from his image of the work done by the nurse in the hospital in which he was trained, and partly by the nature of the personal experience he has had of professional contacts with nurses employed in the community services. This empirical approach is clearly illustrated by an analysis of the work done by the nurses in these two practices, and a study of the results has already led to modifications of the way in which the nurse's services are used.

As a doctor and nurse develop a better understanding of their respective roles, the nurse is likely to be given more responsibility, particularly in the supervision of health and welfare of children and expectant mothers, in prophylaxis, in health education, and in dealing with a wide range of social, economic, and personal relationship problems which form the background of the illness for which the patient has consulted the doctor.

*Detailed statistical tables and analyses are available, on request, from the authors.

When a nurse is working directly with general practitioners as part of a family-doctor team she can be said to have three different roles. First, she relieves the doctor of a number of functions which she is often more experienced than he in performing. Secondly, she enables the doctor to undertake both diagnostic and therapeutic responsibilities which he would otherwise discharge by referring the patient to other parts of the Health Service, particularly the hospital and the community nursing services. Thirdly, by assisting the doctor, she extends, both qualitatively and quantitatively, the personal medical care given to the patients.

We have not attempted here to categorize the various tasks performed by the nurse in this way. This would have involved innumerable subjective decisions which we were not prepared to make. We have simply described the nature of her work in quantitative terms.

The particular practices in which this study was carried out are quite atypical. The salient features of their organization are the existence of a family-doctor team comprising two doctors, a nurse, and a medical social worker; the heavy teaching commitments of all members of the staff; and the small number of patients on the list of each doctor. As they differ from the majority of general practices in so many ways it is quite impossible to ascribe variations in the number and nature of the services provided to any one particular feature. Thus the high consultation rate (6.6 per patient per year) and the low prescribing rate observed may be influenced by each of these three factors.

The relatively high consultation rate certainly suggests that, while the nurse can relieve the doctor of a number of time-consuming duties, her presence in a general practice does not necessarily reduce the overall amount of work performed by the doctor. When he is freed of such tasks as the application of dressings and providing detailed advice and instruction about diet, he is able to assist his patients in other ways. Our description of the treatment provided by the doctors in these practices has shown the considerable extent to which they are concerned with the social and emotional problems of their patients (Scott *et al.*, 1960). In this respect the nurse may well act as a stimulant to the general practitioner. The appreciable amount of discussion between the nurse and the patients often revealed complications and additional problems of which the doctor was made aware at the daily case conference. Fox (1960) has suggested that the particular object of the personal doctor's independent existence may be defeated if he leaves all dressings to the nurse, sympathy to the receptionist, messages to the secretary, and the solution of home problems to the social worker. Our experience does not support this thesis, but suggests that a family doctor working with a nurse may have rather more personal contacts with his patients than one who works on his own and refers more of his patients to the hospital or to any other agency.

Clearly, if a nurse was to work with a general practitioner in a very different situation—for example, where the doctor had a large list and none of the other additional facilities available to the doctors in our practices—the effect might be rather different. It is probable that the nurse would be mainly employed by the single-handed doctor with a large list to relieve him of his more arduous tasks and thus enable him to augment his scanty leisure; but even in such a situation it is likely that he would be stimulated to extend his range of diagnostic and/or therapeutic activities.

Besides enabling the doctor to have more free time and/or time to extend the care given to patients, it is possible that the nurse could enable the doctor to look after a greater number. Our feeling, however, is that this effect is not likely to be large, because the pressure to provide more care or care of a different nature is pretty considerable, and only doctors already overburdened with their commitments are likely to be able to resist it.

We would conclude that the main effects of a nurse working in general practice are, first, to extend the care given to patients; secondly, by relieving the doctor of arduous and time-consuming tasks, to ease his sense of frustration (it might be that "therapeutic listening" to the general practitioner is the most important and most frequent duty of the nurse in this situation); and, thirdly, to reduce the amount of use made of other parts of the Health Service, and in particular the hospitals, district nurse, health visitor, and possibly the pharmaceutical services. Although we feel that this arrangement of a nurse working directly with a general practitioner is in many ways ideal from the viewpoint of the patient, we do not claim that it could or should enable doctors to increase their size of list with impunity.

In various ways the nurse helps to co-ordinate many different services. She does not replace the health visitor or district nurse, but helps to ensure efficient collaboration between them and the general practitioner. To some extent, however, she does relieve them of some of their duties in the same way that the general practitioner, by holding a child-welfare clinic in his practice, relieves the medical officer of health of part of his responsibility. Here, again, closer collaboration between the family doctor and the local health authority services seems likely to increase the extent and improve the nature of care provided rather than to reveal much overlapping of services.

Costs

It may be thought that the system described here, in which one nurse works directly with two general practitioners, is an idealistic one, but that the cost of such a service would be so prohibitive as to make its general application quite unrealistic.

It is not possible to compute exactly the net cost of such a service, since we are unable to estimate the possible saving which would occur in other services. The following facts and figures, however, provide a background against which the proposal can be considered. They relate to England and Wales in 1958.

During that year the hospital and specialist service accounted for 57% of the expenditure on the National Health Service, general medical services for 10%, pharmaceutical services for 10¼%, and the local authority services for 9%. At this time there were 19,685 principals in general practice, 10,189 home nursing staff (51% of them part-time), and 6,393 health visitors, again many of them part-time.

Thus there was a ratio of one health visitor or district nurse to every 1.2 general practitioners, although in "full-time equivalents" it would be more nearly two to every three G.P.s.

The cost of providing one additional nurse for every two doctors, if such nurses were available, would be, at an average salary of £800,* £7,874,000. If this scheme were adopted it would almost certainly be reasonable to reduce the present force of district nurses and health visitors. If they were reduced to one-half of their present level, this would mean that the cost of the scheme would be about £3,937,000. This sum could be realized by a reduction of 1.04% in the cost of the hospital services, and it seems possible that a scheme like this could effect such a saving. It is also possible that this scheme might reduce the cost of the pharmaceutical service. In the practices in which this study took place the average cost per prescription was just slightly below the general average, but the prescribing rate was two-thirds of that in the area. If this rate was general it would effect a saving of £21,800,000—that is, nearly three times that of the *total* cost of providing these additional nurses.

However, the major obstacle to the employment of nurses in general practice may not be expense but shortage of suitably qualified nurses. This type of work is in many ways particularly suitable for nurses who are married and have some family responsibilities, since if a nurse is available during only one consulting period each day it is possible for the general practitioner to organize his work in such a way that he makes the best use of her services. Alternatively, in a large practice it might be possible to employ more than one part-time nurse so that one would be available at each of the consulting times.

Summary

Two general practices, each staffed by two doctors, a nurse, and a medical social worker, were studied for a period of one year. The work undertaken by the nurses in this situation is described and analysed.

In one practice a third of the nurse's work, as measured by the number of consultations, was taken up with antenatal and child-welfare work. In each practice patients consulted the nurse on average approximately once for every four times they consulted the doctor. At just over half the normal surgery consultations with the nurse, patients saw the nurse without the doctor being present.

At the ordinary surgery consultations the nurses performed some sort of therapeutic action at three-quarters of these occasions, some action with a diagnostic purpose at one-quarter, and provided advice, explanation, information, or "therapeutic listening" on just over two-thirds. The application of dressings and therapeutic injections constituted the major part of their treatment, and assisting the doctor at examination and weighing were the most common forms of diagnostic procedure. The nature of the patient's illness, diet, nutrition, and normal physiology were the most frequent topics of discussion between nurses and patients; and at as many as one-fifth of the consultations the nurses recorded that they felt the patient had benefited because they had listened sympathetically while he related his troubles.

The types of condition most often seen by the nurse were skin conditions, pregnancy, child welfare, accidents and injuries, diseases of the eyes and ears and female genital organs, rheumatic diseases, varicose veins, cardiovascular disease, and obesity. Babies, elderly people, and women of child-bearing age were the groups of patients most likely to consult the nurse.

The advantages of this arrangement, the nurse working directly with the general practitioner, were felt

*The present Whitley Council salary scales are £655 to £830 for health visitors and £600 to £775 for district nurse midwives.

by the individuals concerned to be considerable. It is suggested that the main effects are to extend the range of care given to patients, to ease the sense of isolation and general feeling of frustration commonly experienced by general practitioners, and to reduce the amount of use made by these doctors of the hospital, local authority, and pharmaceutical services. Certain calculations suggest it is possible that the wide-scale application of such a system might result in a saving to these last three services which would offset its cost.

This account of a collaborative study would be incomplete if we did not record our indebtedness to the large number of individuals who made it possible. Our thanks are especially due to our two nursing colleagues, Miss Margo Ferrier and Miss Janette Robertson, who, as former members of the staff of the unit, assisted in the planning and collected the appropriate data during the year in which this study was carried out. Mrs. E. Harnden was responsible for the tabulating and computing. A good deal of extra clerical work was undertaken by our secretaries, and in particular by Miss H. P. Pace. Mrs. N. Cheshire and Mrs. J. Gibson did most of the coding and transferred the data to punched cards. Past and present members of the staff of the unit who collaborated in this study included the following:—almoners: J. McNicol, J. E. Paterson, and J. Throne; doctors: J. A. D. Anderson, D. W. Maclean, I. S. McRobbie, D. H. McVie, M. W. Moss, and H. R. Neve. The cost of the study was met by a grant made by the Secretary of State for Scotland on the recommendation of the Advisory Committee for Medical Research.

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British Medical Association

ANNUAL MEETING AND BIENNIAL CONFERENCE OF THE NEW ZEALAND BRANCH, AUCKLAND, 1961

SUMMARY OF PROCEEDINGS

SECTIONS OF OBSTETRICS AND GYNAECOLOGY AND DERMATOLOGY

Thursday, February 9

Leucoplakia and Vulval Atrophy

With Dr. I. B. SNEDDON (Sheffield) in the chair, Dr. H. J. WALLACE (London) read a paper on leucoplakia and vulval atrophy. He said that leucoplakia was a disorder which varied considerably in appearance and he thought that the simplest diagnostic procedure was to observe the histological changes in the mucous membrane during the hypertrophic phase which alternated with the atrophic phase of the condition. Malignant change was likely to occur at any stage and it was important to differentiate hypertrophic leucoplakia from chronic dermatitis and atrophic leucoplakia from lichen sclerosis.

Leucoplakia of the vulva was often associated with intense itching and was confined to the labia minora, clitoris, and inner aspects of the labia majora. There appeared to be no correlation with syphilis or vitamin-A deficiency, but chronic irritation and dermal dystrophy were predisposing factors. It occurred most commonly as a complication of lichen sclerosis or primary atrophy but could arise from a chronic dermatitis or without any obvious cause.

The treatment of the condition was difficult, and the only certain method of removing the risk of carcinoma was to cut out the cancer-bearing areas. These were sometimes difficult to define, and inadequate surgery might be followed by the recurrence of leucoplakia. In general, vulvectomy was indicated after the age of 40. Before this age, or after if vulvectomy was contraindicated or refused, observation should be carried out at two-monthly intervals in order to detect early cancerous changes. It was sometimes possible to secure symptomatic relief by section of the pudendal nerve, but local anaesthetic applications and radiotherapy were not desirable. Topical hydrocortisone and oral antihistamines were the least ineffective symptomatic treatments.

Dr. Wallace then discussed the differential diagnosis of leucoplakia from lichen sclerosis, chronic dermatitis, lichen planus, psoriasis, and moniliasis. He concluded by describing the changes associated with vulval atrophy and suggested that the term kraurosis be discontinued, since it was not clear whether it was used to describe a primary atrophy of the labia minora and clitoris or a benign, involutionary atrophy predominantly of the vestibule and introitus. Atrophy of the labia minora and clitoris was usually potentially sinister. The benign types of vulval atrophy were involutionary, and often inflammatory, changes confined to the vestibule and introitus and senile genital atrophy.

In the discussion Mr. BRUCE W. GRIEVE (Auckland) emphasized the value of multiple biopsy studies as an aid to accurate diagnosis and suggested that the treatment of leucoplakia, lichen sclerosis, or vulval atrophy which was associated with intractable pruritus was simple vulvectomy. In reply to Dr. I. O. STAHLE (Melbourne), who favoured conservative treatment for lichen sclerosis of the vulva at any age, even if accompanied by persistent irritation, Dr. WALLACE said that this might be justifiable if the patient could be seen at two-monthly intervals.

SECTIONS OF OBSTETRICS AND GYNAECOLOGY AND ANAESTHESIA

Friday, February 10

Anaesthesia in Obstetric Practice

With Dr. C. R. CLIMIE (Auckland) in the chair, Dr. W. D. WYLIE (London) read a paper on some aspects of anaesthesia in obstetric practice. He limited the subject to the problems associated with anaesthesia for emergency obstetrics in the labour ward, noting that much of the present interest in it stemmed from the challenging picture presented by the figures for maternal mortality due to anaesthesia in the United Kingdom, and the widespread feeling that anaesthesia for obstetrics had not generally kept pace with that for other branches of surgery. It could be estimated that about 9% of avoidable maternal deaths were related to anaesthesia, and that 60% of these were due to pulmonary aspiration of stomach contents. National figures gave little evidence of morbidity, yet hospital experience suggested that about 4% of mothers in labour vomited during purely inhalational anaesthesia, and that about 1% developed non-fatal pulmonary complications as a result. A survey of anaesthetic practice in the labour ward in the obstetric unit of 40 teaching hospitals and large non-teaching hospitals

in the United Kingdom revealed that local analgesia, typically pudendal nerve block, was favoured for most procedures. Extradural or subarachnoid analgesia was rarely used. When local analgesia was impracticable, purely inhalational anaesthesia had its advocates, but the use of a muscle relaxant, a cuffed endotracheal tube, and minimal inhalational anaesthesia was widely favoured. The last technique, though presenting special risks in the hands of an inexperienced anaesthetist, had marked advantages for the mother and baby. Dr. Wylie concluded that a junior anaesthetist had no place in the labour ward, unless supervised by a senior and experienced colleague.

Dr. C. R. CLIMIE (Auckland), opening the discussion, said that in the National Women's Hospital, Auckland, no death had occurred during forceps delivery due to aspiration of vomit. Pudendal nerve block was used for 71.2% of forceps deliveries, epidural analgesia for 20.5%, and general anaesthesia for 8.0%. Professor GORDON KING (Perth) spoke in favour of controlled spinal analgesia and quoted a personal series of 500 consecutive caesarean sections performed under this form of analgesia without complications. Mr. I. B. FARIS (Auckland) thought that the pudendal nerve block had many disadvantages and sometimes made the obstetrician's task unnecessarily difficult by failing to produce adequate operating conditions. He favoured the advantages of any form of general anaesthesia, provided it was administered by a skilled anaesthetist.

Dr. WYLIE, in reply, favoured Mr. Faris's statement, and noted that in four busy non-teaching hospitals in the U.K. local analgesia was rarely if ever used, as the staff favoured the more ideal conditions produced by muscle relaxant, endotracheal tube, and minimal inhalational anaesthesia.

SECTION OF OBSTETRICS AND GYNAECOLOGY

Friday, February 10

Treatment of Genital Prolapse

With Professor T. N. MCGREGOR (Edinburgh) in the chair, Mr. K. PACEY (Wellington) discussed the treatment of genital prolapse. He began by discussing the supports of the pelvic organs and the anatomy of the urethra, the pouch of Douglas, and the pre-rectal tissues. The supports consisted of the muscular diaphragm inferiorly and the endopelvic fascia above. Consisting of striated muscle, the pelvic diaphragm contracted in response to stretching, and rise in intra-abdominal pressure initiated its retentive function. Failure of the muscular diaphragm allowed the bladder and uterus to slip down between separated or weakened pubococcygeal muscles, stretching the fascial supports as they descended. Repair could be reduced to simple terms: shortening of the elongated fascial ligaments and repair of deficiencies in the muscle layer. Mr. Pacey said that the anatomical lesion producing stress incontinence was severance or elongation of tissues attaching the urethra to the back of the symphysis pubis. Backward sagging of the urethra was increased by coincident failure of the levator mechanism. There had been much recent interest in the part played by the pouch of Douglas in the production of prolapse. Its depth was variable, and, if in a Manchester-type operation a deep pouch be disregarded, a potential hernial sac would persist between the upper vagina and the rectum. A rectocele was favoured by stretching of the vaginal wall, by stretching or laceration of the perineal body, and by stretching or laceration of the fascia propria of the rectum.

The basic operation for repair of genital prolapse was still one of the Manchester type. It was associated with extensive mobilization of the bladder and thereafter it was usual to plicate the overlying pubocervical fascia. This operation, satisfactory for most purposes, was inadequate for a number of complicating conditions. A large cystocele and/or stress incontinence of urine required the additional suture to each other of the pubococcygeal muscles, behind the upper urethra, and beneath the base of the bladder. A deep pouch of Douglas, a potential enterocele, might be dealt with at this stage of posterior colpoperineorrhaphy, or through the posterior fornix when repairing the prolapse, or by the performance of vaginal hysterectomy. A large rectocele, in addition to colpoperineorrhaphy, demanded repair of the disrupted tissues in front of the rectum. Of the recurrent and vexatious problems in vaginal repair, Mr. Pacey considered stress incontinence in the absence of prolapse and cystocele, intractable enterocele, vaginal prolapse after total abdominal hysterectomy, and the question of the patulous introitus. Repair of genital prolapse might be summarized as a replacement of the urethra, restoring its original length; a reduction of stretched and elongated endopelvic fascia; repair of the muscular diaphragm; and the excision of redundant peritoneum.

Professor GORDON KING (Perth, Western Australia) expressed his agreement with the rationale and excellence of what should be called "Pacey's operation." The Manchester-type operation had almost as many variants as it had adherents. He gave a short survey of methods of delivery should pregnancy follow a Manchester-type repair. Mr. B. SHIEFF (Auckland) raised the question of surgical treatment of prolapse in the elderly, and Mr. I. B. FARIS (Auckland) initiated a brief discussion of recto-vaginal and urethro-vaginal fistula. Mr. L. C. L. AVERILL (Christchurch) considered the problem of suture material, and also that of dyspareunia following operation. Mr. J. E. GIESEN (Wellington) spoke of the importance of mobilizing the bladder neck when dealing with stress incontinence, and Mr. T. A. MACFARLANE (Auckland) recommended closer attention to the prerectal fascia in preventing the occurrence or recurrence of enterocele.

SECTION OF DERMATOLOGY

Thursday, February 9

Surgical Treatment of Angiomas

At this meeting of the Section of Dermatology, to which plastic surgeons had been invited, Dr. RUSSELL THOMAS (Auckland) took the chair, and Mr. P. H. JAYES (London) presented a paper on the surgical treatment of angiomas. He had found the following classification helpful: (A) *Flat:* (1) spider naevus; (2) salmon patch; (3) port-wine stain. (B) *Raised:* (1) superficial (strawberry naevus); (2) deep (cavernous angioma). Spider naevus sometimes regressed in children, and often appeared for the first time in adults. Excision of the central area of the naevus was advised and closure by one or two very fine sutures. Peripheral discoloration faded and the scar was invisible. Diathermy often succeeded in removing the naevus but tended to leave a small depressed scar which could not be hidden with cosmetics.

Salmon patch naevus was pink in colour. The surface was smooth and of normal skin texture—usually spread over a very extensive area of the face. Surgery was rarely advised unless the patch was small and situated in a position which allowed complete excision and closure with a favourable scar. Skin-grafting gave a very patchy result and should not be undertaken. As the surface of the naevus was smooth and the colour not intense, these lesions could be hidden satisfactorily with cosmetic creams. Thorium-X treatment sometimes made the naevus paler, but treatment was rather tedious and the results were uncertain.

Port-wine stain was dark-bluish in colour; the skin was sometimes thickened and the surface "warty." It did not regress spontaneously. Small lesions could be excised and the defect closed directly or by local flaps. The only possible treatment for extensive port-wine stains was complete excision in stages and replacement by split-skin grafts. The cosmetic result was often patchy and indifferent, and it was doubtful whether surgery should be undertaken if the surface of the lesion was smooth and flat, as these

lesions could be successfully camouflaged by the use of cover creams. If the surface was "warty" it was impossible to hide the lesion with cosmetics and there was a strong indication for excision. Operation was usually best delayed until growth was complete, and careful planning was necessary to ensure that the edges of the grafts fell into the natural lines of the face. There was sometimes a tendency for small patches of angiomatous tissue to reappear on the surface of a graft or along its edges.

Strawberry naevus and cavernous angioma were usually not present at birth but appeared soon afterwards and often grew rapidly in the first year of life. They frequently regressed—sometimes completely—in the next two to five years. Early treatment was not advised unless the size and situation of the lesion permitted complete excision with an invisible scar; otherwise treatment was delayed until there was no evidence of further regression. Lesions which were truly progressive and invasive were rare, and in Mr. Jayes's opinion far more deformity was caused by over-enthusiastic treatment than by waiting to see if natural resolution was going to occur. Complete regression sometimes resulted in a wrinkled atrophic "scar" which might require excision at a later stage. Cavernous angiomas which failed to regress could often be improved considerably by partial excision. It might not be possible to remove all surface discoloration, but a great improvement in cosmetic appearance could often be obtained by excising a bulky swelling and restoring the affected part to its normal size and contour.

Mr. Jayes said that there was considerable scope for partial excisions. Owing to the formidable appearance of these lesions and the fear of uncontrollable haemorrhage the surgeon was frequently disinclined to operate in cases which could be much improved by the judicious removal of part of the lesion. In other cases there was a tendency for the surgeon to be far too radical because of an ill-founded fear of cutting through angiomatous tissue. The introduction of hypotensive anaesthesia had helped considerably, particularly in adult patients. Excisions could be carried out more quickly with less blood loss, and some cases were now amenable to surgery which would have been considered inoperable previously.

Mr. Jayes then briefly mentioned other methods of treatment, including irradiation, injections of various substances, and tattooing.

In the discussion, Mr. J. J. BROWNLEE (Christchurch) said that injections of boiling water were useful to bring about earlier resolution of strawberry naevi, and Dr. B. H. R. HILL (Napier) stated that he was certain that well-controlled doses of *x* rays should be used at an early stage to produce a similar effect. Dr. I. B. SNEDDON (Sheffield) pointed out the difficulty of assessing the true value of irradiation in view of the fact that a high percentage of strawberry naevi underwent spontaneous regression. Dr. H. C. W. STRINGER (Dunedin) wanted to know at what age surgery should be undertaken to remove the residual deformity when a strawberry naevus had failed to disappear completely. Mr. JAYES replied that operation was usually desirable in the fourth year of life, before the child started school.

Treatment of Basal-cell Carcinomas

Dr. R. D. SWEET (Plymouth) described a very simple treatment of basal-cell carcinomas by curettage and cauterization. He had recorded in some detail the results of personally treating about 450 lesions in this way in the course of the last ten years; 150 of them were treated over four years ago. He recommended it as the treatment of choice for all small basal-cell carcinomas, especially in elderly people, because: (1) it could be carried out on the spot in the out-patient department or the consulting-room; (2) it was almost entirely painless during treatment and afterwards; (3) little, if any, dressing or aftercare was required; (4) the cosmetic results were excellent. The recurrence rate was under 10%, even when lesions over 1 in. (2.5 cm.) in diameter were included. Recurrences could be re-treated the same way with minimum inconvenience and a high likelihood of success. Dr. Sweet said that radiotherapy should be abandoned as a routine treatment for basal-cell carcinomas. Smaller lesions should be treated by curettage or simple excision, depending on their situation. Larger lesions should be excised and grafted, though occasionally curettage and cautery, even in stages, could be carried out with surprising success. Radiotherapy should be reserved for treatment of recurrences if further surgery seemed undesirable or too mutilating.

In the discussion, Dr. F. S. AIREY (Christchurch) said that he sometimes treated basal-cell carcinomas by curettage in a similar way to Dr. Sweet, and that he had been pleased with the results. Dr. A. M. JOHNSON (Sydney) believed that these lesions, like their owners, should be treated as individuals, and he stressed the value of combined clinics in which a dermatologist, a surgeon, and a radiotherapist could discuss these cases together. A better method than the feel of the curette to determine the edge of the lesion was histopathological examination of the excised lesion. He had abandoned the cautery and curette because of recurrences, but favoured the use of *x* rays. Dr. W. M. MANCHESTER (Auckland) said that Dr. Sweet's cases were mostly of a discrete type, but that he personally encountered many infiltrating lesions which were not suitable for curettage. The histological material obtained by curettage did not supply any information about the completeness of the removal.

Cosmetic Dermabrasion

Dr. F. S. AIREY (Christchurch) said that dermabrasion for cosmetic blemishes was now past the experimental stage, and one was concerned more with its special applicability to certain conditions than its use in general, which at first was thought to be wide. The operator encountered a number of obstacles in his path, which was obscured by the psychic and physical composition of the individual patient (and operator). In Australia the climate was "continental," accounting for the prevalence of degenerative changes which should be particularly responsive to dermabrasion.

Sceptics had asserted that dermabrasion was a passing fancy; but modern dermatology was concerned with cosmetics and their patients were "appearance-conscious." Abrasion techniques had overtaken the cosmetician's exploratory activities, and dermatologists, formerly engrossed with cutaneous diseases, were now required to cater for the demands for improved personal appearance. Since they could meet this urge to a greater extent than previously, the undoubted advantages of dermabrasion should be clarified, and in this connexion patient-selection was paramount.

In the discussion, Mr. P. H. JAYES (London) made a plea for the careful selection of cases which would show permanent rather than temporary improvement from dermabrasion. He did not consider dermabrasion useful for the removal of tattoo marks, the majority of dirt-ingrained scars, or pigmented skin lesions, but favoured this treatment for pitted scars resulting from acne.

Plastic Treatment of Naevi

Mr. W. M. MANCHESTER (Auckland) showed a series of patients illustrating the treatment of angiomas, moles, and basal-cell and squamous-cell carcinomas in a plastic unit. Four children were presented who originally had extensive strawberry naevi involving the nose, cheek, upper lip, and pectoral region; in each case spontaneous regression had occurred. Mr. Manchester emphasized again the desirability of a conservative approach in dealing with angiomas. Several cases were shown in which post-auricular Wolfe grafts had been used to replace moles and other small lesions on the face, and other patients were presented illustrating the use of pedicle flaps for more extensive reconstruction of the nose and lips in malignant cases.

Friday, February 10

Clinical Meeting

Under the chairmanship of Dr. H. J. WALLACE (London), eleven patients were demonstrated at the clinical meeting. Dr. H. BLACK (Auckland) presented one case with a history of blistering of the skin at the site of friction which was considered to be due either to porphyria or to acquired epidermolysis bullosa, and another with a 4½-year history of an indurated plaque behind the right ear which proved to be a haemangiosarcoma. Dr. M. PURDY (Hamilton) demonstrated a girl of 5½ years with multiple mesodermal neoplasia most of which appeared to be haemangiomata and lymphangiomata. He also showed a case of calcinosis circumscripta in a woman of 44 years. It was suggested that the abnormality might be part of a systemic scleroderma.

Dr. P. B. FOX (Auckland) presented four cases. Among these was a woman of 25 years who became blind after chloroquine had been used to treat her lupus erythematosus. The dangers of this treatment were emphasized and it was suggested that for superficial lesions local destruction with carbon dioxide snow was preferable. The more widespread use of local prophylactic sunscreen applications was strongly supported. There was also a patient who developed degenerative lesions of the skin on the face and about the mouth and nose at the age of 5 years. Later these changes appeared on the hands and around the eyes. The patient had reached the age of 42 years and there had been a gradual decrease in the size and number of the lesions over the years. Similar changes had been noted on the face, arms, and neck of the patient's father and in 5 of his 12 children. Only one of a third generation of 30 children was known to be affected. Section of the skin showed masses of colloid material in the subepidermal region. Further investigation of this seemingly unique case was planned. Dr. Fox next demonstrated the case of a Samoan boy, aged 10 months, with lipodystrophy. The absence of fat was particularly noticeable in the face. Blood examination showed an iron-deficiency anaemia, and liver biopsy revealed excessive storage of normal glycogen, fatty infiltration, and changes suggestive of early cirrhosis. Finally a case of congenital cutaneous dystrophy was demonstrated and Dr. FISCHMANN (Auckland) presented a case for diagnosis.

Allergic Purpura and Arteritis

With Dr. I. O. STAHLE (Melbourne) in the chair, Dr. I. B. SNEDDON (Sheffield) read a paper on allergic purpura and arteritis. He stressed that not only was the nomenclature of the various vascular allergides confusing but that the clinical features of many of the syndromes overlapped. Their manifestations depended on the size of the blood-vessel involved rather than the cause of the damage. An allergic reaction to carbromal produced an easily recognized eruption, but an identical condition might occur spontaneously as the result of contact allergy or venous stasis. In some ways capillary endothelium behaved like epidermis.

Dr. Sneddon also reviewed the more serious conditions, such as Schoenlein–Henoch purpura and polyarteritis nodosa, between which the dividing line was hazy. The former occurred in the elderly and often followed an exacerbation of a chronic chest infection. He said that the more benign arteritis of dermal vessels described by Ruiter appeared to be identical with Gougerot's nodular dermal allergide, and that as yet no cause for it had been found. Widespread racemose livedo had recently been recognized in association with generalized arterial disease, particularly neurovascular lesions. It was not identical with polyarteritis nodosa, which could be simulated by nodular vasculitis. This appeared mainly in overweight women in whom the only constant abnormal laboratory finding was a raised sedimentation rate.

Dr. A. BETTY FISCHMANN (Auckland) opened the discussion by suggesting that, in view of the advances in understanding of auto-immunity in other fields, this group of diseases would repay investigation from that angle. Dr. H. C. W. STRINGER (Dunedin) had observed a number of cases of vasculitis in hypertensive patients receiving hypotensive drugs, and he considered that the treatment was responsible. Dr. C. H. BELTON (Nelson) described a case of chronic abdominal pain which had mystified both physicians and surgeons until the finding of an increased capillary fragility had suggested polyarteritis nodosa. The diagnosis had been confirmed by biopsy.

Some Rare Disorders

Dr. H. J. WALLACE (London) then presented slides to illustrate rare diseases and recent topics of interest in England. He showed examples of histochemical techniques which had been developed by his colleague, Dr. George C. Wells, in the investigation of tissue enzyme reactions in the skin. Other topics considered were nail changes in lichen planus and alopecia areata, angioma corporis diffusum, the effect of chloroquine on the cornea and retina, and numerous other conditions.

SECTION OF ORTHOPAEDIC SURGERY

Friday, February 10

Minor Orthopaedic Disabilities

With Mr. H. JACKSON BURROWS (London) and Mr. J. S. BATCHELOR (London) presiding, Mr. A. F. DWYER (Sydney) discussed forefoot deformities, particularly hallux valgus complicated by dislocation of the second and third metatarso-phalangeal joints producing metatarsalgia. He advocated open correction of the dislocations with arthrodesis of the interphalangeal joints by means of internal fixation with stainless-steel pins. The valgus deformity of the hallux was corrected by removal of the exostosis, capsulotomy of the first metatarso-phalangeal joint, and osteotomy of the base of the first metatarsal. The foot was immobilized in plaster-of-Paris with the toes in maximum plantar flexion for four to six weeks. For patients with severe hallux valgus he advised arthrodesis of the first metatarso-phalangeal joint.

Mr. HARMAN SMITH (Auckland) emphasized the importance of the early recognition and treatment of club-foot. When the deformity was bilateral he used the Denis Browne splints and plaster-of-Paris for unilateral deformity. When the deformity was resistant to correction he advocated tenotomy of the tendo Achillis. He advocated the medial release operation for patients in whom the deformity recurred. Dr. J. B. MCCULLY (Auckland) discussed ankle sprains, and emphasized the value of local anaesthesia in assessing the severity of the injury. Mr. ALLAN MACDONALD (Auckland) discussed acute knee injuries, and stressed the importance of examination under general anaesthesia. Surgical repair was indicated when there was evidence of rupture of the internal collateral and cruciate ligaments.

Mr. J. R. KIRKER (Auckland) stressed the importance of the early admission to hospital of all patients with symptoms of osteomyelitis. When the response to conservative treatment with antibiotic therapy for 48–60 hours was unsatisfactory, surgery, with drilling of the bone, was indicated. Mr. DENIS KING (Auckland), discussing sprained fingers, said that fragments of bone detached from the bases of the phalanges sometimes developed rotational deformities and required open reduction. For minor sprains he advocated early active movement. Abnormal movement due to severe ligamentous injury was an indication for operative repair, particularly in the first metatarso-phalangeal joint. Mr. W. A. J. PIKE (Auckland) pointed out that mallet finger deformity often caused very little disability. For conservative treatment he recommended splintage with "tubegauz" and collodion for four weeks, with the distal joint straight (not hyperextended) and the proximal joint slightly flexed, followed by protection with "elastoplast" for two weeks.

Mr. O. R. NICHOLSON (Auckland) said that in 79% of cases of de Quervain's syndrome the abductor pollicis longis tendon was double, and in one-third the extensor pollicis brevis was in a separate compartment. Ulnar abduction of the hand, including the thumb, was a reliable diagnostic test. In the carpal-tunnel syndrome trophic changes were occasionally found in the thumb, index, and middle fingers. He found that the results of splintage were disappointing. Mr. W. J. B. MACFARLAND (Auckland) emphasized the need to warn the patient with tennis elbow that injection therapy was sometimes followed by an exacerbation of symptoms. He found manipulative treatment unsuccessful and surgery unsatisfactory. In treating pain in the shoulder due to degenerative changes in the rotator cuff, he had performed osteotomy of the neck of the scapula with success.

SECTION OF PSYCHIATRY

Thursday, February 9

Humour as an Element in Mental Health

With Dr. DESMOND CURRAN (London) in the chair, Dr. S. W. P. MIRAMS (Wellington) said that, although still frequent, jokes about psychiatrists were no longer as fashionable as formerly. When the fashion was at its height psychiatrists tended to be on the defensive and indulged in much "interpretation" of the phenomenon.

The distinction between wit and humour was difficult, but in general wit demanded more verbal skill and intelligence; humour was more human. The study of an individual's sense of humour yielded clues to his personality structure and psychopathology, as well as indicating personal, social, and cultural attitudes. Recovery from mental illness could sometimes be traced in the re-emergence of a sense of humour. The humour centred round mental health betrayed its origin in the unconscious of its exponents.

Humour might help the patient—and his doctor—to take themselves less seriously. It should not always be interpreted as evidence of latent aggression or hostility. A mature specialty should be capable of laughing at itself. Indeed, the capacity to laugh at oneself might be an index of professional as well as personal maturity.

In discussion Dr. D. CURRAN (London) suggested that it was possible to adopt the opposite view—that a sense of humour could be harmful to mental health, and gave the example of the alcoholic in whom this trait might lead to catastrophe. Professor W. H. TRETHOWAN (Sydney) described a patient who was enabled to work through a difficult transference situation by writing competent humorous verse about psychiatrists. Dr. H. BOURNE (Dunedin) questioned whether humour was an index of maturity. He felt it was a curiously overvalued personality trait which might become evident only in severe mental illness such as mania, and disappear with recovery. He mentioned that patients sometimes lost their ability to be witty after psychotherapy—though improving in other respects.

Psychiatric Evidence in Court

Dr. D. CURRAN (London) stated that though the best psychiatric evidence should be available in British courts this was not the case at present. Many psychiatrists avoided giving evidence whenever possible, one of the most important reasons being the amount of time consumed. The present judicial procedure was not designed to obtain an accurate psychiatric assessment of a prisoner. Significant sections of a psychiatric report were frequently ignored, so that the psychiatrist was forced to subscribe to an incomplete and therefore inaccurate view. The habit of solicitors who touted round various psychiatrists until they obtained the opinion they wanted had been harmful to the profession. In court, psychiatrists were often asked unanswerable questions, and the position, which was bad enough under the McNaughton rules, was immeasurably worse since the passing of the Homicide Act of 1957, which introduced the concept of diminished responsibility. The definition of psychopathy in the Mental Health Act of 1959 was likely to lead to further difficulties.

Psychiatric evidence would probably be called for more frequently in the future, and it would seem advisable that cases should be remanded to mental hospitals or, better still, to special centres linked to psychiatric units rather than to prison as at present. Another source of difficulty was that the psychiatrist was not privileged and might have to disclose confidential information under cross-examination. This raised obvious ethical difficulties. More privilege, at any rate in civil actions, should be accorded to doctors.

Dr. V. YOUNGMAN (Brisbane) described how in Queensland it was difficult to convince a court that a patient might be malingering. Dr. CURRAN (London) replied that the capacity of most people for self-deception was so great that they had no need to malinger. In such cases one could only point out to the court that no organic cause was present, and that it was difficult to be sure how much the patient was deceiving himself and others. Professor W. H. TRETHOWAN (Sydney) emphasized this same difficulty. Dr. C. S. MOORE (Seacliff) described the procedure in New Zealand. In serious cases the prosecution, at an early stage, asked for an opinion by one of the psychiatrists employed by the Mental Hygiene Division. In appropriate cases this led to certification and admission to hospital without the long delays occasioned by attendance at court, so that early treatment could be achieved. Dr. CURRAN commented on the fact that in Britain juries often tended to disregard the McNaughton rules, and that the curious anomaly existed that there was no appeal against a verdict of unfit to plead. Professor W. H. TRETHOWAN (Sydney) mentioned that the unethical habit of a psychiatrist sitting in attendance upon a barrister, in order to advise him how best to embarrass the opposition, had been discouraged by the Australian Association of Psychiatrists.

New Zealand Black Magic

With Professor W. H. TRETHOWAN (Sydney) in the chair, Dr. L. GLUCKMAN (Auckland) spoke of Makutu, the black magic of the New Zealand Maori. "Leaders of a primitive society," he said, "may use magic and mysticism to cover their own ignorance, and the pre-European Maoris provided no exception." Their view of the beginning of the world was a vast expanse of darkness and water inhabited by Io. Io created life and separated the waters, and in the process Rangi, the Sky Father, and Papa, the Earth Mother, appeared. From these developed all forms of life, but the breath of life issued from Io. Rangi and Papa embraced and had 70 children, but they remained so close together that no light could penetrate between them, and their children lived in cold and darkness. One of their offspring, Tane, proposed to force the parents apart, but not all the children agreed. Tane, however, led a successful revolt and thus represented life personified and became the fertilizer of Maori myth. The opposition to Tane was led by Whiro, who represented darkness and evil. After a long and difficult struggle Whiro was defeated and compelled to stay for ever in the underworld, where he initiated and organized all human evil. His emissaries were the Maiki brethren, who personified disease and waged a constant war against mankind. Here, in the House of Death of the spirit world, black magic originated. Hine-Ahu-One, the first woman, was endowed with ability, benevolence, and industry by two of Whiro's brothers, but Whiro himself endowed her and all her issue with the sum total of the evils of mankind. Thus in the first mortal woman the forces of good and evil were already at war.

Whiro himself was represented in this world by the lizard, and to the Maori the lizard symbolized death. If the gods decided to destroy man, the lizard could be introduced into his body and cause disease or death. Such a view precluded advance in medical knowledge. Io was supreme, and Papa and Rangi and their children were second-class or departmental gods. A third class were the tribal deities who personified natural phenomena, and the fourth type were the Atua Maori, or the spirits of the ancestors, who could

be placated. These last two types of god could be interpreted by a human medium, and they were the powers that made the black arts effective.

The status of the priest of each group corresponded with the importance of the group, priests of the lower group being nearer to the common conception of witch-doctor or charlatan. Priests were known as Tohungas, and the term comprised the meanings of expert and teacher. The Tohunga Makutu was a medical wizard, and to him the superstitious Maori was an easy prey.

Tapu

From the gods came a series of "Thou shalt nots" (Tapu), breach of which led to the withdrawal of the divine protection, leaving the individual exposed to innumerable and ever-active evil principles. Tapu lay over the Maori from birth to death, and when it was broken the individual was left defenceless. Dr. Gluckman described how Makutu could be practised by the recital of spells. There were counter-spells to these, but the Maori could never know when he was at the mercy of evil influences, and the gift of food or of a garment might spell his death warrant. Accidental trespass over a Tapu place might have terrible consequences, and it was therefore possible to bury some such medium as a trap so that the person walking over it might break the Tapu and be consigned to the power of evil. Makutu could not be associated with the lofty culture of Io. The magic arts which were taught in Whiro's underworld were represented on earth by the Whare Maire. In this place instruction in magic took place at night. Doctrinally, Makutu was a fall from grace, a negative result of the withdrawal of the divine protection as a consequence of Tapu violation. But this teaching was corrupted and Makutu became a positive and active evil. The witch-doctor encouraged this view and used spells and incantations to fortify his own position in society.

Dr. Gluckman said that the Maori of to-day still related illness and misfortune to Makutu. In chronic disease it might be difficult to persuade the patient that he was not the victim of a spell. In reversible or transient conditions when the recovery took place a similar explanation was readily accepted. Dr. Gluckman recalled cases of epilepsy ascribed to breach of Tapu in which any freedom from seizure was ascribed to the power of the Tohunga. He gave case histories illustrating these points and also showed how resistant to rational therapy such patients and their families might be. His cases showed, moreover, that resignation to inevitability robbed the patient of a powerful force tending to recovery. One girl predicted her own death, and when it took place no organic reason could be found for it. Christian teaching theoretically accepted, and imposed upon Maori myths, in more than one of the cases given was little protection from the power of Makutu suggestion or from the feelings of guilt aroused by a breach of Tapu. Higher education also was unable to prevent belief in witchcraft. A Maori who had studied advanced psychology and anthropology still attributed his own anginal pains to Makutu.

If credence was to be given to Jung's concept of a collective racial unconscious, then it had to be recognized that the modern Maori was very close to primitive history unconsciously as well as consciously. Dr. Gluckman expressed his belief that present-day Makutu was a transitional cultural phenomenon whose components were a rationalization of guilt, fear, superstition, and ignorance with a sentimental desire to cling to the past. Many of his patients who had suffered from Makutu had great pride in their Maori origin. The decline of Maori culture after the advent of the white man was followed by the renaissance of a modified mythology. Magic rituals of recent date incorporated Old Testament as well as Maori custom, and the angel Gabriel had appeared to a Tohunga. The Ringatu faith, in which faith-healing still played a large part, was supported by both Biblical and Maori reference, and similar sects had been formed. True Maori knowledge in New Zealand had declined, and the majority now inherited the worst of their background, Io being forgotten and sickness and misfortune being interpreted in terms of witchcraft. The situation was comparable to that of Europe in the Middle Ages.

Dr. RINA MOORE (Nelson) recalled her own Maori childhood. She had no fear, only reverence, of her religious inheritance. Religion in pre-European days took the place of common law, and it was difficult to draw a line between white and black magic. Dr. L. I. SHENKEN (Auckland) pointed out that obsessional personality traits and superstitions were very prominent among Europeans. Dr. R. F. P. GRACE (London) expressed the view that since the Maori wars the pattern had greatly altered. Some leaders fostered beliefs that supported their crumbling status, perhaps abusing their position in a way that was formerly unnecessary. Dr. C. A. CORBAN (Auckland) cited the "super science" and astonishing credulities of European peoples to-day, including belief in astrology and superstitions of all kinds. Dr. D. I. M. SINCLAIR (Tolaga Bay) spoke as a physician who treated many Maoris. In chronic disease they would rationalize their lack of progress and seek the Tohunga (or the colour therapist) to offset the failure of medical treatment.

Friday, February 10

Some Aspects of Alcoholism

With Dr. DORIS ODLUM (Bournemouth) in the chair, Dr. J. J. CRAWSHAW (Auckland) read a paper on some aspects of alcoholism. Alcohol, he said, offered a welcome escape from the tensions of everyday life. The incidence of addiction was increasing in many parts of the world, and it was estimated that in New Zealand there were between 15,000 and 20,000 chronic alcoholics. Neurotic subjects, the physically deformed, psychopaths, and sometimes the psychotic provided fruitful soil for the development of alcoholism. Those who drank excessively might be classified as (*a*) constant heavy drinkers, (*b*) the abnormal routine drinker who drank steadily and regularly without becoming overtly intoxicated, and (*c*) compulsive drinkers who often indulged in secret and often attempted frantically to break the habit.

The willing co-operation of the patient was a *sine qua non* of successful treatment. Adverse criticism merely deepened his resentment, and attempts limited to modifying the intake of alcohol were bound to fail. The patient must have resolved to avoid alcohol completely. Initial hospitalization was advisable to permit control of withdrawal symptoms, to initiate psychotherapy, and to allow contact with Alcoholics Anonymous. Chlorpromazine had proved valuable in controlling withdrawal symptoms, but barbiturates and paraldehyde should be avoided. Aversion therapy, psychotherapy, and hypnotherapy all had their place in appropriate cases. Disulfiram, though not a specific form of treatment, was a valuable safeguard against relapse. Alcoholics Anonymous, by employing group methods, achieved undoubted successes. The members of this organization carried out active field work and brought their ideals to the notice of untreated alcoholics. A proportion of chronic alcoholics could be salvaged, and a spirit of tolerance, sympathy, and understanding was essential to detect them and promote their recoveries.

Dr. D. ODLUM (Bournemouth) inquired what facilities were available in New Zealand for the treatment of chronic alcoholism. Dr. J. J. CRAWSHAW replied that in addition to mental hospital facilities a hostel for alcoholics seeking employment had just been opened. There was also an "inebriates' island" to which alcoholics could go voluntarily or following committal by a court. In reply to Dr. L. K. GLUCKMAN (Auckland) Dr. Crawshaw suggested that the minimum period of "drying out" an alcoholic should be a week, but that it was important to balance one's judgment carefully, as patients became resentful if kept too long. Chronic alcoholics admitted to a mental hospital should remain at least three months. He commented that faith was probably an essential of cure, but it did not have to be religious faith. Atheism was compatible with recovery. Dr. D. T. CLOUSTON (Wellington) commented on the wide-

spread flouting of the strict licensing laws in New Zealand, which, he felt, encouraged alcoholism. Professor W. H. TRETHOWAN (Sydney) speculated on the pathophysiology of the blackouts, periods of amnesia, and episodes of automatic behaviour that accompanied alcoholism. Dr. CRAWSHAW felt that psychological factors played an important aetiological role in these conditions, though some might have a vascular basis. Dr. C. S. MOORE (Seacliff) wondered if a case could not be made out for the compulsory detention of alcoholics at an earlier stage than was at present possible, so that treatment could be given before the patient and his family were ruined.

Epilepsy and the Community

With Dr. D. CURRAN (London) in the chair, Dr. RINA W. MOORE (Nelson) said she was primarily concerned with epilepsy as a personality disorder, and the way in which epileptics reacted to their disease. It was important to consider the possibility of epilepsy in any child who showed temper tantrums followed by a deep sleep, and E.E.G. records might be of real value in such cases. Much depended upon the way in which doctors advised parents about their epileptic children, in order that a course should be steered between the dangers of over-protection on the one hand and "rejection" on the other. In New Zealand attempts were made to integrate epileptics into the community rather than to segregate them. It was often helpful to explain to the other children before an epileptic child first went to school what might happen, so that they might be forewarned. Sufferers from epilepsy were specially liable to meet reactions of fear and horror, and in their turn to react with asocial or paranoid attitude. Epileptics ran the risks of maladaptation of any minority group, and there was much need for a broad educational programme to counteract ignorance and fear. Special problems arose in connexion with driving licences, the eugenic risk as regards children, and employment. On the whole, the public were unduly concerned about the risk of epilepsy in children of epileptic parents. Dr. Moore was specially interested in epilepsy among Maoris. It was in her experience very uncommon in the Maori population, and some of her race claimed it never occurred in a full-blooded Maori.

Status of Encephalography

A lively discussion followed Dr. Moore's paper. Dr. D. T. CLOUSTON (Wellington) suggested that the bad odour in which electroencephalography found itself might be due to the dependence of many departments upon their technicians, who even reported upon the records. Single brief recordings were often valueless, and the investigation required careful planning. It was important that full clinical details should be available when records were interpreted and that the statistical nature of many E.E.G. reports should be appreciated by clinicians. Electroencephalography was helpful in elucidating cases of epilepsy when only a poor history was available from relatives, and was a valuable method of investigation in cases of petit mal.

Dr. G. L. GLASGOW (Auckland) said that in his experience the E.E.G. was of very little value in cases of epilepsy, and in this and other fields not more than one record in ten provided worth-while information.

Dr. L. G. KILOH (Newcastle upon Tyne) pointed out that it was often the misplaced enthusiasm of the interpreter that caused difficulty rather than the method itself. The E.E.G. had a very definite place in the diagnosis of epilepsy, but many clinicians did not appreciate its limitations, and were disappointed when they learnt that it could not be employed to exclude epilepsy or other conditions. Over-optimistic interpretations of non-specific abnormalities had also caused great harm. In focal epilepsy, particularly when the temporal lobe was involved, the E.E.G. could provide essential information unobtainable in any other way.

Professor W. H. TRETHOWAN (Sydney) blamed the enthusiasm of psychiatrists in particular for the present status of electroencephalography. He stressed its value in the diagnosis of cerebral tumours and its role in detecting cases presenting with schizophrenic symptoms but which in fact suffered from temporal lobe epilepsy.

SECTION OF OPHTHALMOLOGY

Friday, February 10

Light-coagulation Therapy

With the president, Mr. FRANK LAW (London), in the chair, Mr. GRAEME G. TALBOT (Auckland) read a paper on light-coagulation therapy. He described the technique of operating the Zeiss light coagulator, essentially a complicated electrical ophthalmoscope, and discussed the conditions in which it was of value. He said that when the intense light from the coagulator was focused upon an opaque substance such as the choroid it was immediately transformed into heat. It was necessary, therefore, for the operator to be protected by a dark glass which rose in his ophthalmoscope field before contact was made, even though exposure was only continued for ½ to 1 second. When the light coagulator was used for the treatment of macular holes a localized choroiditis, similar to that seen in an eclipse burn, was produced. The method was simpler, more accurate, and less destructive than diathermy. With peripheral holes, which should be closed at once, a higher intensity of light was required whether or not there was detachment of the retina.

Those patients with a detachment who were treated by surgery should be observed daily in the post-operative period so that light coagulation could be employed as an accessory to surgery if necessary. Light could also be applied to the area of the separation after local scleral resection and drainage of a retinal cyst. In the case of a retinal foreign body it was applied around the edge of the foreign body before removal. The coagulator could be used to treat malignant melanoma of the retina in persons over 60 years of age and could be combined with *x*-ray therapy in the treatment of secondary carcinoma. Patients with angiomatosis retinae, angiomata of the choroid, and retinoblastoma should also receive light-coagulation therapy. A patient with a big retinoblastoma should probably first receive *x*-ray therapy and treatment with nitrogen mustard, and in those cases where more than a third of the retina was involved light coagulation was not practicable.

If another attachment was made on the arm of the instrument to focus the light at a distance of about two inches an iridectomy could be produced in an "updrawn" pupil, and it was also possible, under these conditions, to treat tumours of the iris, epitheliomata at the limbus, xanthelasma, and blood-vessels growing into a pterygium.

Discussion

Opening the discussion, Mr. A. F. FERGUSON (Wellington) asked what dose should be given in superficial lesions like epithelioma. Mr. TALBOT replied that repeated light doses were better than heavy dosage, and suggested an initial dose of 1 second. He said in answer to Mr. D. C. MACDIARMID (Hamilton) that there was no timer on the machine. Mr. F. LAW suggested that, as macular holes and peripheral retinal cysts so often gave rise to no complications, the necessity for their treatment at all should be carefully weighed. He thought the method was of great use in cases of peripheral holes where detachment was threatened but not actually present, and he issued a warning against coagulating vessels for fear of haemorrhage; more research was necessary in this direction. He also doubted whether light coagulation would ultimately prove of much value in cases of malignant melanoma and retinoblastoma where excision was not indicated; Eade's therapy seemed more effective.

Dr. G. de L. FENWICK (Auckland) asked how the method acted in devascularizing the cornea; presumably there was sufficient blood pigment for absorption to occur. Mr. RANDALL ELLIOTT (Wellington) wondered whether a condensing lens and sunlight might not be equally effective.

As there was possibly a solar element in the aetiology of pterygium, he doubted whether light coagulation was a suitable treatment. Mr. C. PITTAR (Auckland) felt that one should hesitate before treating a macular hole because there was a real risk of enlarging the central scotoma. Mr. D. T. SHORTBRIDGE (Sydney) said that in view of the increasing efficacy of established methods of treatment of detachment of the retina, he questioned whether light coagulation would play an important part.

NATIONAL ASSOCIATION FOR MENTAL HEALTH

MR. POWELL ON THE FUTURE

The annual conference of the National Association for Mental Health was held in London on March 9 and 10. It took as its theme "Everybody's Business: Emerging Patterns for the Mental Health Services and the Public." The Minister of Health, Mr. ENOCH POWELL, who opened the conference, spoke on the relationship between the 10-year hospital plan which he had announced earlier in the year and the future of the mental health services.

Fifteen Years Ahead

The essential idea of the plan, he said, was to assess the hospital provision which was thought right and practicable for the mid-1970's. Such an assessment was nothing less than a forecast and expression of intention embracing the future of all branches of the National Health Service, indeed of the nation's provision for health as a whole. He had intimated to the hospital authorities who would be producing the constituent elements of the national hospital plan that in 15 years' time there might well be needed not more than half as many places in hospitals for mental illness as there were to-day. In numerical terms, this represented a redundancy of no fewer than 75,000 hospital beds. "But that 50% or less of present places," said the Minister, "what will they look like and where will they be? We know already what ought to be the answer to that question: they ought for the most part to be in wards and wings of general hospitals. Few ought to be in great isolated institutions or clumps of institutions, though I neither forget nor underestimate the continuing requirements of security for a small minority of patients.

Asylums of Our Forefathers

"Now look and see what are the implications of these bold words. They imply nothing less than the elimination of by far the greater part of this country's mental hospitals as they stand to-day. This is a colossal undertaking, not so much in the new physical provision which it involves, as in the sheer inertia of mind and matter which it requires to be overcome. There they stand, isolated, majestic, imperious, brooded over by the gigantic water-tower and chimney combined, rising unmistakable and daunting out of the countryside—the asylums which our forefathers built with such immense solidity. Do not for a moment underestimate their powers of resistance to our assault. Let me describe some of the defences which we have to storm. First there is the sheer physical solidity of the buildings themselves: the very idea of these monuments derelict or demolished arouses an instinctive resistance in the mind. At worst, we find ourselves thinking, can't we use them for something else if they cannot be retained for the mentally ill? 'Why not at least put the subnormals into them?' 'Wouldn't this one make a spendid geriatric unit, or a convalescent home.' 'What a pity to waste all this accommodation!' Well, let me here declare that, if we err, it is our duty to err on the side of ruthlessness. For the great majority of these establishments there is no appropriate future use, and I for my own part will resist any attempt to foist another purpose upon them unless it can be proved to me in each case that such, or almost such, a building would have to be erected in that, or some similar, place to serve the other purpose, if the mental hospital had never existed there.

Hospitals are not Pyramids

"We have to strive to alter our whole mentality about hospitals, and about mental hospitals especially. Hospital building is not like pyramid building, the erection of memorials to endure to a remote posterity. We have to get the idea into our heads that a hospital is a shell, a framework, however complex, to contain certain processes, and, when the processes change or are superseded, the shell must most probably be scrapped and the framework dismantled. The old Roman virtue of *pietas* becomes a vice when it is directed towards a hospital building. Much of what we have done in the last decade to improve these mental hospitals has made the right course from now on more difficult still. . . . There comes a point where the very improvement of existing facilities militates powerfully against their supersession by something different and better. The resistance is not only physical. Hundreds of men and women, professional or voluntary, have given years, even lifetimes, to the service of a mental hospital or a group of mental hospitals. . . . From such bodies it demands no mean moral effort to recognize that the institutions themselves are doomed." The transformation of the mental hospitals, continued the Minister, was not only a matter of buildings or the change of a physical pattern, it was also the transformation of a whole branch of the profession of medicine, of nursing, of hospital administration. Politics apart, everyone had a great deal of the conservative in his make-up, and found it easier to envisage things going on much as at present, than deliberately to choose and favour the unaccustomed and the drastic, and voluntarily to bring about a pattern of organization in which new tasks would be performed in a new and wider setting.

Prospects for Subnormal Patients

When looking at the future of provision for the subnormal, the prospects for change must seem far less dramatic, certainly when one discounted the chance of a medical "break-through" on this front. Far from contemplating the certainty of a heavy run-down in numbers, we had to reckon with the increase which flowed automatically from the increased expectation of life of subnormal people and their improved prospects of surviving infancy.

Community Services

Speaking of the community services, the Minister went on to say that a hospital plan made no sense unless the medical profession outside the hospital service would be able progressively to accept responsibility for more and more of that care of patients which to-day was given inside the hospitals, and could be supported in this task by a whole new development of the local authority services for the old, the sick, the mentally ill, and the mentally subnormal. "That is why," added Mr. Powell, "at the earliest moment possible, I intend to call on local health and welfare authorities, through the bodies which represent them, to take a hand in mapping the joint future of the hospital and the local authority services."

Limiting Factors

This year capital expenditure of local health and welfare authorities had been fully half the capital expenditure on the hospital service, and it was expected that something like that ratio would be maintained. What was needed urgently was not money but a much clearer and more definite statement than we yet possessed of the need, and the provision for it, at which local authorities were aiming. In fact, the community counterpart of the long-term hospital plan ought to be as effective a formative and driving influence outside the hospital service as the hospital plan itself was inside. In 1961 it was intended to erect the initial scaffolding of a professional training for the social worker, and to link that with the training of other elements

(*Continued at foot of next page*)

To-day's Drugs

With the help of expert contributors we publish below notes on a selection of drugs in common use.

Spiramycin

"Rovamycin" (May and Baker).

Composition.—Spiramycin is an antibiotic obtained from culture-filtrates of *Streptomyces ambofaciens*. Chemically it consists of a mixture of organic bases with similar physical, chemical, and biological properties, but its exact constitution has not yet been elucidated. It is a cream-coloured, odourless, amorphous powder, and when dry is stable on exposure to light and air. The base is soluble in most organic solvents.

Antibacterial Spectrum.—Spiramycin can be classified in the erythromycin–oleandomycin group of antibiotics. It is especially active against Gram-positive bacilli and *Neisseria*, and is relatively inactive against Gram-negative bacteria. There is some bacterial cross-resistance between erythromycin, oleandomycin, and spiramycin, especially for staphylococci.

Pharmacology. — Spiramycin administered orally is incompletely and irregularly absorbed, particularly in young children. The concentration of the antibiotic achieved in the cerebrospinal fluid is about two-thirds of the corresponding blood level, and the amount of active material excreted in the urine, while varying considerably, does not exceed 10% of the ingested dose.

Therapy.—Spiramycin should be employed only when an infection is proved to be caused by an organism which is sensitive to it and insensitive to erythromycin and other antibiotics in common use. Its empirical use should be discouraged because of its inconstant absorption and the tendency to produce cross-resistance to erythromycin, which is the most effective antibiotic of this group. It is administered orally in tablets or capsules of 250 mg., and in those few cases where its use is justified—e.g., staphylococcal enteritis with strains resistant to erythromycin and other antibiotics—it should be given to adults in doses of 3 to 5 g. daily and to children in doses of 75 to 100 mg./kg. daily. It is absolutely contraindicated as the sole agent in the treatment of meningeal infections.

Toxic Effects.—Very few have been reported. They including nausea and vomiting, epigastric discomfort, diarrhoea, and skin reactions.

N.H.S. Basic Price.—20 tabs. 18s. 4d., 20 capsules 21s. 8d.

(*Continued from preceding page*)

in the staff of the community services. Without widespread public understanding and resolve, concluded the Minister, the planners might plan and the administrators administer, but the face of the map would not be changed.

Discussions

In a speech made on the second day of the conference Professor R. M. TITMUSS, professor of social administration at the London School of Economics, called for three acts of policy as proof that the Ministry of Health's statements of intention were to be taken seriously: the first was a grant to local authorities of £10m. for 1961–2, specifically for community care for the mentally ill and subnormal; the second was central Government grants for all social work students and training courses, irrespective of specialty, in the universities and technical colleges, and the establishment of courses in 15 colleges by October, 1962; the third was a royal commission on the recruitment and training of doctors, with special reference to the need for education in social and psychological medicine.

During the course of the conference there were speeches on "Integration," "Treatment in Hospitals," "Community Care—Fact or Fiction," and "Public Attitudes," and much formal and informal discussion.

Correspondence

Corticosteroids and Dermatological Diagnosis

SIR,—One of the most difficult problems for the dermatologist is to detect the factors which give rise to or maintain an eczematous dermatitis. When this is primarily exogenic in origin the diagnosis may often be made only by correlating exacerbations of the disease with exposure to some irritant, often quite unsuspected by the patient and only determined by a long and carefully taken history. Similarly, with an essentially constitutional eruption one may be able to discover the major causal factor by associating periods of exacerbation with specific physical or psychological stresses.

The advent of corticosteroids has greatly increased the problem of diagnosis. An exacerbation of eczema may now be due to stopping or merely reducing the dose of the steroid, or it may be that the patient has neglected to take his tablets for a day or so. Thus the diagnosis is greatly confused, since the "flare-up" may be quite unrelated to the major cause of the rash. Furthermore, corticosteroids do not deal with the source of the disease but only suppress the symptoms, and here again serve only to obscure the true diagnosis. Where possible, steroids should not be used until a complete aetiological diagnosis has been made, though I realize this is often not feasible.

More important, and the real object of this letter, I would ask that when a patient who has been on corticosteroids is sent to a dermatologist for an opinion, he should always be accompanied by the exact details of his steroid treatment, including the dosage and the dates of any variation in this. Too often one has to rely on some vague statement from the patient about having his tablets changed; this did not matter so much when it was changing from one sedative to another, but corticosteroids are a very different matter.—I am, etc.,

Leeds General Infirmary, Leeds. F. F. HELLIER.

National Epidemiology

SIR,—The idea of a central register of personal records relating to health, such as that suggested by Dr. E. D. Acheson, Dr. S. C. Truelove, and Professor L. J. Witts (March 4, p. 668), has attracted Somerset House from time to time ever since the days of Farr himself. It became less visionary with the introduction of the National Health Service, but the cost, practical difficulties, and possible objections probably remain greater than your correspondents suggest, despite the potentialities of electronic storage.

Nevertheless, we would not want to rule out the possibility of such a register, although it would probably have to be organized on a sampling basis. We feel that the views of other correspondents might help to show how great an effort ought to be put into overcoming the difficulties, and we would welcome any comments on the matter.—I am, etc.,

Somerset House, London W.C.2. M. A. HEASMAN, Acting Chief Medical Statistician, General Register Office.

SIR,—The letter from Dr. E. D. Acheson and his colleagues (March 4, p. 668) draws welcome attention to the benefits which could be gained from proper use

of the by-products of the National Health Service. In this country we have unique opportunities deriving not only from the National Registration Number, allocated to every individual, but also from the existence of medical "lists" of people for whose care general practitioners are responsible.

More widespread use of the N.H.S. Number could be made in general practice as well as in hospital. As only two-fifths of all deaths take place in N.H.S. hospitals,[1] a place might well be found for the N.H.S. Number on the death certificate and cremation certificate forms. The personal medical cards designed to be carried by patients have borne the National Health Service Number since 1948, but these are often mislaid. Medical record envelopes, originally designed in the early 1900's, do not always carry the N.H.S. Number when they are received from executive councils, and sometimes lack the age also. A new look should be taken at personal medical documentation, in all its aspects, so that it may become an effective research tool.

The College of General Practitioners has, after considerable discussion and experiment, designed a standard summary card for use within the N.H.S. recording system. This card at present contains space for some of the items listed by Dr. Acheson and his colleagues, and could be adapted to hold more. It could be used to provide the "domiciliary" medical history of the patient to complement that from hospital sources.

The Research Committee of the College has already brought into being the embryo of a unit designed to handle information collected by the use of record-card, episode-card, ledger, and other techniques. This unit, to be developed in collaboration with the Birmingham Regional Hospital Board, will study methods of electronic storage and statistical analysis of information. Information thus gained can be added to information accumulated during the running of the continued morbidity studies of the unit,[2] and would serve to check the accuracy of sampling methods based on general medical practices, the age and sex structure of which is exactly known. It is known that age–sex registers have now been completed by 35 members of the College Research Register, and that number increases steadily.

The College welcomes the suggestion that concerted efforts be made to secure official support for the study of epidemiology through the National Health Service, and its records unit will be willing to join with others in work to this end. It is pleasant to record that the College records unit, like the department of clinical medicine at the Radcliffe Infirmary, from which this challenge comes, owes its support to Lord Nuffield's generosity.—I am, etc.,

Birmingham.

R. J. F. H. PINSENT,
Chairman, Research Committee of Council.
The College of General Practitioners.

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1 Glyn Hughes, H. L., *Peace at the Last*. A Survey of Terminal Care in the U.K. A Report to the Calouste Gulbenkian Foundation, London. 1960.
2 *J. Coll. gen. Practit.*, **1**, 107.

Kwashiorkor

SIR,—I read with interest the article in your issue of December 17 (p. 1759) by Drs. Joan Scragg and Carol Rubidge. At the beginning of their very full paper on the malnutritional syndrome of kwashiorkor, they stress the strictness of their criteria in diagnosing this condition. Later on in the paper they record their impressions on the corneal lesions as seen by them. *Inter alia*, the condition of "malnutritional keratoconjunctivitis" as described by me in a paper in 1950[1] is mentioned in the following words: "We prefer to apply the term keratomalacia to the corneal lesions in our cases rather than Blumenthal's name—keratoconjunctivitis."

Not one of the many thousands of cases of malnutritional keratitis (as I subsequently renamed the condition) seen by me could by any stretch of the imagination be said to have shown any of the stigmata of kwashiorkor. If Drs. Scragg and Rubidge will read two further papers on the subject,[2 3] they will realize that malnutritional keratitis has little clinical relationship, if any, to either kwashiorkor or keratomalacia. In my second paper I listed 10 clinical differences between keratomalacia (as summarized by Duke - Elder[4]) and malnutritional keratitis.

I must touch, too, on their use of the term "ulceration" of the cornea. This cannot apply to malnutritional keratitis, where I proved (I hope) conclusively that ulceration in its pathological sense does not occur, except as a later infective and relatively unimportant complication. I feel, therefore, that for them to apply the name keratoconjunctivitis to what they have seen in kwashiorkor is both inappropriate and incorrect.—I am, etc.,

East London,
South Africa.

C. J. BLUMENTHAL.

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2 —— ibid., 1954, **28**, 967.
3 —— *Proc. Nutr. Soc.*, 1960, **19**, 92.
4 Duke-Elder, W. S., *Textbook of Ophthalmology*, 1938, vol. 2, p. 1754. Kimpton, London.

SIR,—Drs. Joan Scragg and Carol Rubidge in their article on kwashiorkor (December 17, p. 1759) have covered the clinical aspects most ably. With regard to aetiology, however, the article gives the impression that the problem is peculiar to the urban African, and Durban in particular. The King Edward VIII Hospital, in which the series was seen, although situated in Durban, attracts patients from all over rural Natal. In a survey conducted by my department in December, 1959, and January, 1960, it was ascertained that of 364 diagnosed kwashiorkor cases admitted during that period, only 42 (11.5%) were domiciled in Durban. The majority by far of the remainder came from rural Bantu reserve territories in Natal and Zululand.

Of the contributory factors in such cases the more important are illegitimacy, ignorance and tribal superstition, and impoverished soil. Here is a common picture taken from my African investigator's report:

"There are two or three daughters at the kraal: the courting man in each case works in a city, usually Durban or Johannesburg. He pays one or two beasts as part-payment of 'lobola' (dowry). The woman has a child but her father will not consent to marriage until the final beast, usually the eleventh, has been paid. The Bantu in the city refuses to keep on paying and deserts. The other daughters in turn suffer the same fate. The father, getting older, now finds he has to support his wife, three daughters, and three illegitimates; however, his funds are quite insufficient to take the extra load and before long members of the family suffer from kwashiorkor, tuberculosis, and other deficiency states.

"A similar situation arises in the case of an unmarried rural girl who becomes pregnant. Father demands two beasts for 'damages.' The man refuses and does not visit the kraal again. The daughter does not work, and has to

be supported as well as the growing child; as the money will not go round the child falls a prey to malnutrition."

With regard to the urban African, illegitimacy again is a major factor. To quote again:

"The fact that so many of the child sufferers are illegitimate is a vital factor in the problem. This is because, according to Bantu custom, the father of an illegitimate child has no responsibility whatever for the support of the child, and he will not recognize any obligations beyond his payment of two beasts if his paternity is proved. The welfare of the child becomes the responsibility of the parents of the mother. To go further than this and to make the issue a legal one is so involved and complicated that this further step is seldom undertaken. The man feels quite at liberty to take another woman, beget other children, and again disclaim all responsibility.

"On the mother's side, when the 'lover' abandons her she often does her best to get another man to help support her; another illegitimate arrives and often the new man does not want to support the other fellow's child and in consequence it becomes neglected."

The fact that the urban incidence is so much lower than the rural is probably accounted for by the fact that mother and baby (child health) clinics and health education are provided by this local authority on a comprehensive scale. These go far towards combating ignorance in regard to feeding methods, and, as Drs. Scragg and Rubidge point out, clinics are a centre for the distribution of supplementary foods. The ultimate remedy does not lie, however, in the provision of supplementary foodstuffs, the burden of which must be borne by the taxpayer, but rather in the rehabilitation of African family life and moral outlook, whose disintegration is so well described by Laura Longmore in her book, *The Dispossessed*.—I am, etc.,

City Health Department, Durban, Natal. A. STEPHEN, City Medical Officer of Health.

REFERENCE

[1] Longmore, Laura, *The Dispossessed*, 1959. Cape, London.

Tooth Reimplantation

SIR,—I was interested to read the letters by Dr. R. R. Stephens and Dr. J. H. Sowray concerning the reimplantation of teeth and reference to the Boyle–Davis gag (January 21, pp. 207 and 208). I had been accustomed to using the Boyle–Davis gag before coming to North America, and am aware of the problem of possible damage to the incisor teeth. Since coming to Canada I have been introduced to the McIvor gag, which is a similar instrument in construction and principle, but simpler than the Boyle–Davis. The pressure of this gag is exerted on the tongue and on each bicuspid region of the upper jaw, and it is easy to use in edentulous patients. I am quite converted to its use and recommend it highly.—I am, etc.,

The Peterborough Clinic, Peterborough, Ontario. PHILIP COLE.

Spontaneous Rupture of Umbilical Hernia

SIR,—Following the report by Drs. S. Brandon and D. Whitehouse (December 31, 1960, p. 1935) that only nine cases of spontaneous rupture of infantile umbilical hernia could be traced in the literature, and recording a further case, I think it may be worth while describing another case.

A 4-year-old well-nourished girl of Bantu stock was seen at Yakusu Hospital in the Congo two hours after spontaneous rupture of an umbilical hernia which had been present since birth. Seven cm. of soiled omental tissue was protruding from a split 1 cm. in diameter at the apex of the hernia. The surrounding skin was healthy. Trauma was denied. Débridement, ligation and excision of the soiled omental tissue, and a Mayo repair were carried out, with uneventful recovery.

Infantile umbilical hernia is commonly seen in the Congo. Local custom includes the encouragement of such hernias in babies; they are apparently a sign of beauty, and feature frequently in primitive sculpture. In view of the prevalence of these hernias, and the thinness of the integument over them, it is surprising that rupture is so rarely seen.—I am, etc.,

London S.E.9. EDWARD H. WYATT.

Phenylbutazone and Leukaemia

SIR,—Dr. R. H. D. Bean's report (November 26, p. 1552), describing cases of myeloblastic leukaemia after phenylbutazone treatment is of particular interest to me, as I have made observations of a similar nature.[1–3] The drugs seemingly responsible in my collection of cases were analgesics containing mostly an aminophenazone derivative, including phenylbutazone and sometimes also phenacetin. A considerable proportion of patients in a series of myeloblastic leukaemias habitually took drugs of this group, either repeatedly or for long periods, for pains which were present long before the onset of the blood disease. Observations were also made on the bone-marrow damage due to these drugs, and the possible transition from a toxic granulocytopenia to frank myeloblastic leukaemia. In a simultaneous series of cases with chronic myeloid leukaemia (i.e., mature cell-type leukaemia) there was no suggestion of a toxic agent as a cause of the disease.—I am, etc.,

R. SCHEUER-KARPIN.

Departments of Medicine and Clinical Pathology, Hufeland-Krankenhaus, Berlin-Buch, Germany.

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[3] —— *Transactions of the Sixth Congress of the European Society of Haematology, Copenhagen, 1957*, 1958, Part 2, p. 214. S. Karger, Basel, New York.

Oral Treatment of Diabetes

SIR,—In your leading article (January 21, p. 188) you pointed out that the real value of the hypoglycaemic agents could only be assessed once their influence on the "all-too-frequent development of vascular disease, retinopathy, and nephropathy" is known.

No doubt all workers who deal with large numbers of diabetics are impressed with the high incidence of these complications, whether the patients are being treated by diet alone or with insulin as well. There is no good evidence that insulin itself, now used for many years, lessens the incidence or severity of vascular disease except in so far as an improvement in diabetic control, however attained, appears to do so on a statistical basis. In our own clinic we have observed a roughly doubled incidence of diabetic retinopathy—for example, in patients with "poor" control—while patients on insulin actually showed a greater incidence than those not on insulin.[1]

Concerning oral treatment in diabetes, we have been impressed with the following findings in successfully treated maturity-onset diabetics: (1) The excellent

control which has been obtained in a large percentage of diabetics who achieved (*a*) normal fasting blood glucose levels, (*b*) urine which was free of sugar throughout the day. (2) The control with oral therapy is often far easier and may be more uniform than with insulin. (3) There is a smaller tendency to hyper- or hypo-glycaemia than with insulin. Where there are fluctuations in the patient's insulin requirement, insulin-induced hypoglycaemia may have serious consequences. (4) A proportion of the diabetics treated with hypoglycaemic agents developed a normal (or near normal) glucose-tolerance curve. This was found in 14 patients out of 35 patients thus investigated.[2] The last finding was surprising to us, since the generally held view is that there is no change in the form of the glucose-tolerance curve.[3]

Do not the above observations suggest that we may be approaching a more rational method of correcting the metabolic error(s) conducive to the development of diabetic angiopathy ?—We are, etc.,

JOSEPH B. HERMAN.
W. P. U. JACKSON.
Diabetes Clinic,
Department of Medicine,
Groote Schuur Hospital and University of Capetown.

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[2] Herman, Joseph B., thesis, University of Capetown, 1960.
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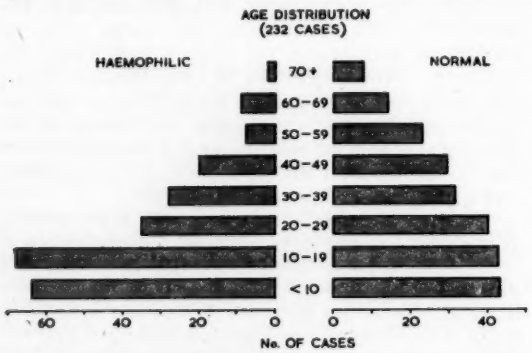
Longevity of Haemophiliacs

SIR,—The report[1] of a family, a haemophiliac member of which lived until the age of 61 years, brought me inquiries regarding the life expectancy of patients with haemophilia or Christmas disease. May I be allowed to supply the following data on this subject ?

Age Distribution.—This was investigated in 232 unselected cases of haemophilia (194) and Christmas disease (38), which was the entire number of living cases registered in 1959 at Manchester Haemophilia Centre. These patients came from Lancashire, Cheshire, Yorkshire, and North Wales. The corresponding age-distribution for the same number (232) of the general population was calculated from the Registrar-General's figures. Fig. 1 was constructed from the results obtained



in these two groups. This figure shows less patients in the older age-group, thus suggesting that most haemophiliac subjects die at an earlier age than the rest of the population. Although this may be accepted as the main factor, it is by no means the only reason for this difference in age-distribution. The following points should be considered: (*a*) Some of the older patients are not willing to visit hospitals or even their family doctor except when confronted with an alarming bleeding episode. (*b*) Mild cases, with no spontaneous lesions,[2] particularly those with no apparent family history, may remain undetected until abnormally reacting to trauma or surgery. My belief that these are two important contributory factors is derived from and supported by the ages of the *new* patients with haemophilia and Christmas disease registered during 1958 and 1959 at Manchester Royal Infirmary (Table I). Many previously unrecognized patients in the older age-groups are still coming forward.

TABLE I.—*Age of New Patients Registered*

Age Group	1958	1959
Under 2 years	6	4
2–10 ,,	8	6
11–25 ,,	5	4
26–44 ,,	0	9
45–60 ,,	2	2
70 ,,	1	0
Total	22	25

TABLE II.—*Causes of Death in Haemophilia and Christmas Disease (Patients at Manchester Royal Infirmary, 1932–59)*

Cause of Death	No. of Patients	Age Range
Alimentary-tract bleeding	7	8–59
Retroperitoneal haemorrhage	3	8–30
Intracranial haemorrhage*	5	9–69
Respiratory obstruction	2	54 and 61
Operative (appendicectomy and hemi-colectomy)	2	24 and 45
Heart failure	1	78
Road accident	1	62

* Case history established that trauma preceded and was apparently responsible for the bleeding in at least 2 cases.

Causes of Death.—These are shown in Table II in 21 cases. These were patients whose death was ascertained and recorded at the Manchester Royal Infirmary during the period 1932–59 inclusive.

I have no doubt that the present life-expectancy will alter as our knowledge grows and methods of treatment continue to advance.[3 4] In order that future workers may be able to detect the importance of this change, it would be necessary to have information from a wider section of the haemophiliac population, estimated at well over 1,500 in this country.[5] This could easily be made available by the Haemophilia Committee (Medical Research Council) by seeking the co-operation of the different haemophilia centres under their aegis.—I am, etc.,

F. NOUR-ELDIN.
Blood Transfusion Centre,
Brentwood, Essex.

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[5] —— Seventh European Congress of Haematology, 1959, Abstract No. 180. London.

Vagotomy for Peptic Ulcer

SIR,—Your leading article (February 25, p. 564) gives a very incomplete picture of this particular problem. Several of the papers which you quote are those in which the results of the work of several surgeons have been pooled together, and therefore they give no idea of the results which are obtainable in clinics where this operation is being done frequently. There is no doubt that vagotomy as a treatment for duodenal ulcer has come to stay, and the only argument is to decide which is the best drainage operation with which it should be combined.

I should like to draw your attention to the results obtained by Feggetter,[1] who reports an incidence of stomal ulceration of only 1% in 600 cases and in the same number of cases recurrent duodenal ulceration in less than 1%. In my own series of 600 cases[2] the mortality rate is 0.5% and the incidence of stomal ulceration about the same figure.

Burge and his associates[3] have in my opinion grossly overestimated the importance of diarrhoea as a complication of vagotomy and gastro-jejunostomy. The incidence is no greater than that following gastro-jejunostomy alone or a Billroth 2 type of gastrectomy. In our series we have no very troublesome cases of diarrhoea. In those patients in whom it occurs it usually consists of short attacks with long free intervals. Most of the cases of diarrhoea have begun some time after discharge from hospital with a history typical of the acute entero-colitis which is so common in this country to-day.

We have yet to find any evidence that vagotomy is responsible for any serious gastric disturbance apart from gastric retention which occurs if it is not combined with a drainage procedure. There is a steadily growing mass of evidence to support the view that most of the post-cibal symptoms following partial gastrectomy, vagotomy, and posterior gastro-jejunostomy, and gastro-jejunostomy alone are due to the anastomosis of the stomach to the jejunum. In an article which is now in the press a ten-year follow-up of 100 cases of duodenal ulcer treated by vagotomy and gastro-enterostomy shows an incidence of recurrent ulceration of 0.5%, but with an incidence of gastric disturbance slightly less but very similar to those following partial gastrectomy.

Burge's test for the completeness of the vagotomy[4,5] we have found time-consuming and not completely reliable. It is nothing like so sensitive as a post-operative insulin fractional analysis. Equally until we can be certain that we are obtaining a complete vagotomy in all our cases it is difficult to make out a good case for the selective vagotomy which Burge advises. Our experience suggests that the best drainage procedure to combine with vagotomy is excision of the anterior half of the pyloric sphincter.—I am, etc.,

Manchester 13. R. L. HOLT.

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2 Holt, R. L., ibid., 1959, **52**, 837.
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4 —— and Vane, J. R., ibid., 1958, **1**, 615.
5 —— and Clark, C. G., ibid., 1958, **2**, 741.

SIR,—Your leading article on this subject (February 25, p. 564) seems to miss the point. You quote figures for recurrence rates after vagotomy and gastroenterostomy, but make no reference to previous acid levels.

I feel that it is important to have the result of an augmented histamine test meal before deciding on the form of surgery for duodenal ulcers, as this will show some cases which are unsuitable for this operation because their acid level is rather higher than that of the duodenal ulcer case. These, of course, are the very cases who are at hazard for a recurrence and who would be better treated by vagotomy and partial gastrectomy.

For this reason, I contend that recurrence rates figures without evidence of previous acid levels must be assumed to include cases who have been wrongly treated. Because of this the operation cannot be considered to be at fault, only its application.—I am, etc.,

Nocton Hall Hospital, Lincoln. J. A. D. J. CUNNINGHAM

Phenazocine and Respiratory Depression

SIR,—Phenazocine ("narphen"), an analgesic, is being advertised as a suitable adjunct to general anaesthesia. Before this advertisement appeared I had used phenazocine instead of pethidine and found that certain cases had severe respiratory depression, requiring nalorphine to restore adequate respiration and then a change of analgesic agent. So I had ceased to use it. I have now tried phenazocine again, and I have kept a record of twenty consecutive cases, using it on healthy adults having orthopaedic or varicose-vein operations.

Premedication was pethidine 100 mg. and atropine 0.6 mg.; or "omnopon" 22 mg. and scopolamine 0.44 mg.; or just atropine 0.5 mg., and does not appear to have influenced the results. All the cases received a sleep dose of thiopentone and then settled with nitrous oxide/oxygen before the respirations were counted and blood-pressure taken. Sometimes gallamine triethiodide was added in small doses when a relaxant was needed. Phenazocine, 1 mg. intravenously, was then given and the respirations counted regularly.

No further phenazocine was given unless the stimulus of the operation required it. Four cases required no further phenazocine. Two of these had very depressed respiration. When required, 0.5 mg. doses were added. Eight cases out of 20 had respirations drop to eight or less per minute. Three of these dropped to two or less respirations per minute and had assisted respiration. Three cases had respirations drop to 9/min. One of these dropped to 8/min. after the operation was over. The remaining nine cases were satisfactory. It was necessary to add trichloroethylene or halothane to ten cases because of movements or shock.

Phenazocine does not seem to cause any important change in blood-pressure, and there was a pleasant absence of post-operative vomiting. However, for maintenance of anaesthesia phenazocine is too unreliable, causing respiratory depression too much.—I am, etc.,

Leamington Spa, Warwickshire. RONALD SHAW.

John Hunter on Artificial Respiration

SIR,—Thanks to the excellent B.M.A. Library, I have had an opportunity of improving my understanding of the physiology of artificial respiration. Hunter's observations are quite in keeping with modern ideas. He suggested[1] a pair of bellows with two separate cavities, one for blowing fresh air in, and one for sucking used air out.

He was well aware that "the influence of the air can act through the coats of the vessels," but goes on to add,[2] "When I was injecting the lungs of a man, the injection did not run freely; I then inflated them, and found that the injection immediately ran with freedom." Thus by artificial respiration we improve very considerably the pulmonary circulation as well as aerating the capillaries, and this must help enormously where the circulation must be near zero in the almost drowned, and this aerated blood getting into circulation may save the patient.

I quote another observation of his which is quite in accord with modern thought: "Every part of the body sympathizes with the mind; for whatever affects the mind, the body is affected in proportion."[1]—I am, etc.,

Shrewsbury. ALBERT E. NICHOLLS.

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2 —— *Essays and Observations on Natural History, Anatomy, Physiology, Psychology, and Geology*, 1861, Vol. I, p. 124. Van Voorst, London.

Medicine in North America

SIR,—May we congratulate Dr. H. J. Cronhelm (January 21, p. 194) on his excellent and unprejudiced account of medical practice in Canada? He is to be complimented on the expeditious manner in which he acquired such a full and accurate picture. His enthusiasm for practice in Canada should not, however, lead one to believe that there are no shortcomings in the present system, nor in those who abuse it. Canada needs, and will undoubtedly soon obtain, a "tax-supported" medical scheme.

As ones who have endured the frustrations and injustices of both the hospital and general medical services of the British N.H.S. before emigration, we sincerely hope and believe that Canada, profiting by the experiences of other countries, can and will find a national health plan both beneficial to her people and acceptable to their doctors. In Canada to-day an honourable doctor can practise medicine fully and with satisfaction whilst receiving a fair reward for his genuine efforts on behalf of his patients. May the good features of Canadian medical practice—namely, the independence of the individual doctor, free choice of doctor for the patient, admission of the general practitioner to the hospital staff, equality of status between all specialists as well as the general practitioner on the hospital staff, partial payment for medical services by the individual receiving them, and the "fee for service" principle—be preserved in any future health service here.

Perish all bureaucratic "capitation" systems, and salaried hierarchies. Long live the "freedom of medicine" (in Canada at least).—We are, etc.,

Nanaimo, B.C., Canada. J. MERVYN THOMAS.
ERIC COOPER.

Anglo-American Medical Society

SIR,—Dr. Thomas Gardner's letter (March 4, p. 673) condemning what he calls "transatlantic mud-slinging" is to be applauded. As he observes, articles such as that by Dr. W. W. Fulton (January 28, p. 275) and those in a similar vein published by the A.M.A. do little to promote understanding between the medical profession of the two countries. That a desire for such understanding exists on both sides of the Atlantic is shown by the interest that has been aroused by a society concerned with promoting a closer liaison and understanding between British and American doctors.

The Anglo-American Medical Society was formed in June last "to promote a close social and professional liaison between the American doctors in East Anglia and their British colleagues, and to examine more closely attitudes, values, and customs as they apply to medicine in both countries." The need for the society was felt to be particularly great in East Anglia because of the large number of doctors of the United States Air Force stationed in the area, as well as Americans engaged in study and research at Cambridge University.

Meetings on topics of mutual interest have been held every other month and have been attended by gatherings of from 100 to 200 doctors—remarkably large attendances for this area. The society also serves as a medium through which American doctors are invited to take part in the activities of local medical societies and Divisions of the B.M.A. It has organized visits to places of medical interest for the American doctors, and a joint Anglo-American research project has already been initiated through it. It is not a body organized by British doctors for American visitors, but is a truly joint enterprise governed by a committee of doctors of the two nations—in fact, our present chairman is an American physician.

We are, of course, a very young society, and have not been able as yet to commence a programme of exchange visits between our two countries. But we are already realizing by our meetings and discussions together that the differences between us are not so great as one is often led to believe, and that they are often caused by ignorance of the true facts on either or both sides.

Although it has never set out to be anything more than a modest local organization, interest in the society has not been limited to East Anglia, and several members have travelled to Cambridge for meetings from as far afield as London, Surrey, and Warwickshire. Many doctors from all over the country have expressed interest in our aims and activities, and, as the result of a small paragraph announcing the society's formation in the *J.A.M.A.*, numerous requests have been received from all over the United States from doctors who wish to share in our activities on the other side of the Atlantic.

In view of this enormous interest, the society's committee sought the advice of national medical organizations (including the B.M.A.) and of other organizations concerned with promoting Anglo-American relations. Following this advice, it is proposed to start additional groups of the society in London and Oxford during the next two or three months, and in New York and Boston, Massachusetts, at the end of the year. I have recently been appointed as the society's first full-time secretary-general, and I will be very pleased to provide full details of our activities to any interested doctors who care to write to me at this address.—I am, etc.,

March Road, Wimblington, Cambridgeshire. ALEC J. EDEN,
Secretary-General,
Anglo-American Medical Society.

Myxoedema with Elephantiasis of Eyelids

SIR,—With the letter by Mr. G. Wishart Hoare and Dr B. Gupta (November 26, p. 1604), there is a photograph of a woman with myxoedema with elephantiasis of the eyelids. The picture bears a striking resemblance to that of a woman seen at Stanford University with Dr. Eugene M. Farber, in whom a diagnosis of cutis hyperelastica with myxoedema was made. I wonder if this could not be the situation here. I doubt a relationship between the two diseases other than coincidental.—I am, etc.,

U.S.A.F. Aerospace Medical Center, Lackland Air Force Base, Texas. JACK D. NOYES.

Depression

SIR,—I read with interest Dr. William Sargant's article, "Drugs in the Treatment of Depression" (January 28, p. 225), and should like to make the following comments.

Regarding the combined use of imipramine and monoamine oxidase inhibitors, Dr. Sargant says, "Here, however, there is naturally a greater risk of postural hypotensive effects and other complications." There is already literature suggesting that the combined use of these two types of drugs is fraught with danger, so much so that the companies concerned now mention it in their literature. Cases of high temperatures, comas, and convulsions have been mentioned, and certainly more articles will appear in the literature in the near future.

In discussing the monoamine oxidase inhibitors, Dr. Sargant mentions that postural hypotension and giddiness is a frequent side-effect, and this may mean having to lower the dose. This is indeed so, but I have found it useful to stretch the dose so that, say on a four-times-daily regime, two tablets are taken at bedtime. This is again now being recommended by the pharmaceutical houses. Dr. Nathan S. Kline has for a long time now been using ephedrine in cases like this. A somewhat lower dosage than is normally used may be necessary because of the potentiating effect of the monoamine oxidase inhibitor. A case here in the last few weeks may be of some interest from this point of view. A severely depressed manic-depressive ambulant male was put on phenelzine, the dosage being gradually increased to 90 mg. day. Due to a snowstorm, he was not seen for two weeks; in the meantime he had made a rapid improvement, and had been out of the house for the first time in months and had actually reached the stage of applying for jobs. In the meantime he developed dizziness and faintness and on seeing his G.P. was noted to have a systolic blood-pressure of 80. His G.P. rightly attributed this to the medication and stopped it at once. When the patient was next seen, he was again depressed, had not gone out, and had given up looking for a job. He was placed again on phenelzine combined with ephedrine, gr. ¼ (16 mg.), twice a day. Within ten days of recommencing treatment he was again feeling much better and was again able to go and search for employment. His systolic blood-pressure remained at just over 100. It has certainly been my experience and that of others that, until a response is obtained from the anti-depressant drug, the combination of an anti-hypotensive medication with the antidepressant drug is a useful adjunct in the treatment of depression.—I am, etc.,

Department of Mental Hygiene, State of New York, U.S.A. GEORGE SIMPSON.

SIR,—Dr. William Sargant is to be congratulated on his article, "Drugs in the Treatment of Depression" (January 28, p. 225). His references to the atypical depressive illnesses, which occur so frequently in general practice and prove to-day so eminently treatable, prompts me to plead with him to accept these for what they are, *formes frustes* of classical melancholic disorder, better termed (as they have been) melancholia minor,[1 2] rather than to confuse the issue by attempting to equate them with "hysterical" types of depressive illness or "anxiety hysteria."

The unfortunate sufferers from melancholia minor are, as Dr. Sargant states, patients of known good previous personality who have become emotionally disturbed, without loss of insight; who, though they wake no earlier yet are unrefreshed after sleep which is characteristically disturbed; and who may have lost a great deal of weight without any organic illness to account for this or any other of their psychosomatic symptoms.

It is of the utmost importance that the general practitioner should learn to discriminate between endogenous melancholia minor whose aetiology, natural history, and response to antimelancholic drugs (and E.C.T.) are so very similar to "big brother" melancholia major (the big difference being in the quantity, so to speak, of the melancholia, the quality remaining the same), and the host of hysterical, reactive, and neurotic illnesses which *may* have a component of depression but which require the emphasis on tranquillization, chemical and psychological, and environmental manipulation.—I am, etc.,

Johannesburg. MAX FELDMAN.

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Alcoholic Content of Drinks

SIR,—Dr. S. E. Josse (February 18, p. 503) is, of course, quite right when he points out that alcohol alone is not responsible for *all* the general effects of drinks. He quotes brandy and absinthe as examples of drinks containing substances such as essential oils, esters, and so forth, but absinthe is fortunately not procurable in this country, and brandy is not a very common tipple.

An accurate description of drinks in terms of alcohol would surely be useful in the case of practically all the beverages which are commonly consumed, in which the ether, ester, higher-alcohol, and essential-oil constituents are not a paramount factor. My object is to encourage intelligent use of alcoholic drinks, and even if there can be no rigid guide to potency on an alcoholic volume percentage basis, by and large such knowledge of strength would be a useful indication to very many people.—I am, etc.,

Broadbridge Heath, Sussex. GUY BOUSFIELD.

Brucella Puzzles

SIR,—Dr. G. E. Breen (February 25, p. 587) writes that he never finds a positive agglutination test among his cases of unexplained pyrexia. It may be that the laboratory technique requires revising, or at any rate a chat with the bacteriologist might help him. There is no need to fall back on blood and bone-marrow culture, and in any case these are less likely to be rewarding. The next useful step is to perform a brucellin skin test, and brucellin is available at all public health laboratories. It is performed in the same manner as a Mantoux test, but the interpretation is a little different. First, it should be read daily for a week, as some patients react very slowly. I suspect this happens in the chronic smouldering type of the disease. Next, it may be negative even though the patient has the disease. Fortunately this can often be detected by the fact that the injection will produce a rise in agglutination titre or by a change from negative to positive. This reaction reaches a peak after 10 to 14 days or sometimes even longer. It does not occur in those who have not been infected. A modification of this test, using a Heaf gun and concentrated brucelline, is reliable, as I have described elsewhere.[1] Skone[2] has also used it.

Brucellosis is certainly a disease of puzzles. I think it is quite likely, as Dr. Breen suggests, that thanks to our age-long parasitism on the cow we have become tolerant of *abortus*. But, as he also hints, pasteurization has eradicated it in urban areas. I am sure that the age-long tolerance is dying away and we are on the threshold of a new era in which people are growing up with no immunity to *Brucella*. In such people the first meeting with the disease may be quite spectacular. This is liable to happen in city dwellers who go on holiday in the country, camping or caravanning and consuming raw milk for the first time in their lives. I have recently seen two cases where the home milk supply was perfectly safe, but the disease was contracted on holiday in the

Isle of Wight, an area where Skone[2] found that 6.3% of churn samples from 520 registered dairy herds were infected with *Brucella*. The disease may not come to notice until many months or even years later, when the holiday milk supply has been long forgotten. Therefore in obscure cases of fever, arthritis, depression, lassitude, etc., it may be worth inquiring carefully into past holidays.—I am, etc.,

Bath. HUGH WALLIS.

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2 Skone, J. F., *Human and Animal Brucellosis*. Royal Society of Health Symposium on Brucellosis. In press.

Treatment of Psychoneuroses

SIR,—Dr. S. Sament (January 21, p. 211), referring to the comparison made in my book[1] of results of treatment by behavioural methods with those of psychoanalysis, writes: "Dr. Wolpe's cases appear to be of the milder emotional disturbances which he calls 'psychoneuroses,' whereas it would appear that the cases treated by psycho-analysts also include those of more severe emotional upsets." This statement suggests that the effects of behavioural methods on psychoneuroses were inappropriately compared with the effects of psycho-analysis on a wider range of conditions. However, it is unequivocally stated, in the relevant chapter of the book, that, while therapeutic methods based on principles of learning have yielded favourable results in nearly 90% of cases of psychoneuroses, the comparative figure for psychoanalysis *for the same group of conditions* is of the order of 50% despite a much larger average number of interviews. It is worth noting that, unlike the psycho-analysts, I have taken on all psychoneurotic cases for treatment, rejecting none.

I agree with Dr. Sament that properly controlled comparative studies are necessary. All that I have claimed is that *as far as the evidence goes* behavioural methods appear to be more effective than psychoanalysis in the psychoneuroses. It is a claim that is getting increasing support.[2]—I am, etc.,

JOSEPH WOLPE.

University of Virginia Hospital, Charlottesville, Virginia.

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Resurgence of V.D.

SIR,—Dr. C. S. Nicol's suggestion (February 18, p. 445) for the use of the description genito-urinary physician instead of venereologist is timely. The word venereal is correctly often equated with sin, yet many as we know who have been exposed to a venereal disease have been guilty only of having parents or a marital partner with one of these conditions. My experience, working in an area where there is little movement of population and where emigration is at a minimum, is that over 85% of married women who contract syphilis or gonorrhoea in marriage do so from their legal spouse. I see no constructive reason why these women and their issue should be forced to live under the shadow of the word venereal; surely it is more than enough that they are labelled as suffering from the name of the disease concerned.

There might of course be justification for the continuance of the terms in use if transmission of the main diseases concerned were confined to sexual contact, but is this so? I do not think it is. The basic common denominator surely is intimate contact, of which genital sexual contact is but one example. Are we not too sex-obsessed when we insist on emphasizing the sexual aspect of transmission in a disease which may continue if uninterrupted by treatment to pass through at least two generations and involve a third, or of a disease which may infect the eyes of a baby in its passage through the vagina, or the vagina of a child who is unfortunate enough simply to share a bed with an infected adult? We would admittedly, if given the opportunity, now limit transmission by means other than illicit sex, but surely we do not normally describe medical conditions by their behaviour as modified by treatment.—I am, etc.,

Belfast. F. S. BONUGLI.

Epidural Anaesthesia and Bed Rest in Sciatica

SIR,—We have just read with interest the article of Dr. E. N. Coomes (January 7, p. 20) and the letter of Mr. F. C. Dwyer and Mr. F. Howard Beddow (January 28, p. 286) on the use of epidural injections in the treatment of sciatica. We feel that our limited experience may be of interest.

During the past year we have treated 27 cases of sciatica by lumbar epidural injection of large volumes of normal saline. The saline was injected slowly until the patient complained of continuous pain in the sciatic distribution. The volume of fluid injected varied between 70 and 100 ml. Of the 27 cases, 19 had immediate relief or improvement of the sciatic pain, but in all but three the relief was temporary, lasting up to four hours.

Of these three cases, two suffered from spondylosis of the lumbar spine with radiating pain in the sciatic distribution and with signs of root irritation, and the third was a patient who had undergone four months previously removal of the posterior arch of the fifth lumbar vertebra for spondylolisthesis. In this patient sciatica had developed some days after the operation for the first time and became progressively worse. It was accompanied by reduction of the straight-leg raising to 50°, hypoaesthesia in the L5–S1 distribution, and loss of the ankle jerk. It was considered that the nerve-root irritation was due to post-operative adhesions, and the complete relief of pain was obtained by the mechanical action of the saline in displacing the dura and nerve-root sheath and in disrupting the adhesions. In the spondylotic cases, which improved with epidural injection, it was postulated that a similar mechanism was involved. In these cases the sciatica is probably due to involvement of the nerve roots by the osteophytic process as they pass through the intervertebral foramina. Again, the displacement of the nerve-root sheaths and disruption of adhesions could account for the relief of pain.

It is interesting to note that in 16 of the cases who experienced relief of pain after the injection there was a concomitant increase of the straight-leg raising and reduction of the lumbar muscle spasm. Severe headache or dizziness occurred in over half of our cases, due to increased intracranial pressure. However, in all cases these symptoms were transient and disappeared within

15 minutes of completion of the injection. No other complications were encountered.

Our limited experience would suggest that the place of epidural injection in the treatment of sciatica should be limited to those cases in which the pain is due to nerve-root adhesion rather than to simple pressure by a prolapsed disk.—We are, etc.,

GORDON ROBIN.
J. T. DAVIDSON.

Departments of Orthopaedics and Anaesthesia,
Hadassah University Hospital,
Jerusalem, Israel.

Is Thalidomide to Blame ?

SIR,—The possibility of peripheral neuropathy as a toxic manifestation of thalidomide (" distaval ") therapy has been raised by Dr. A. L. Florence (December 31, p. 1954) and subsequently referred to by Dr. E. V. Kuenssberg and others (January 28, p. 291).

Two of my patients, receiving thalidomide, developed neurological features. The first was a female aged 74 who received a nightly dose of 100 mg. After nine weeks she began to complain of paraesthesiae and numbness of the hands ; she became querulous and depressed, and constantly rubbed the hands and fingers in an attempt to obtain relief. Unlike the cases of Dr. Florence the lower limbs were unaffected and there were no colour changes. Neurological examination was negative and the C.S.F. was entirely normal. At this time the communication of Dr. Florence appeared ; the drug was immediately discontinued and within a few days there was a remarkable improvement, both in the degree of the disturbing sensations and in the mental outlook. However, there has been persistence in much lesser degree of the paraesthesiae, even after the lapse of seven weeks.

The second patient, a female aged 46, presented with cramping pains and numbness of the lower limbs and a grossly unsteady gait. The essential physical findings were marked sensory ataxia and absence of ankle jerks. There was a history of chronic alcoholism. Total abstinence was advised and vitamins prescribed. Steady improvement occurred, and examination four months later showed no ataxia, but the ankle jerks were still absent. For almost two years the patient had taken a nightly dose of 400 mg. thalidomide. Her difficult personality had prevented her medical practitioner from reducing the dose and she has persisted with the usual dosage in spite of his warning of a possible connexion between the drug and her neurological disorder.

If thalidomide is to be incriminated in the first case, it would appear that the drug is capable of inducing the changes within a relatively short time. Individual idiosyncrasy to the toxic effects is suggested by the events in the second case. Here a patient suffering from alcoholic neuropathy had been able to tolerate the remarkable dosage of 400 mg. nightly for some two years without apparent further damage to the peripheral nerves, as judged by the satisfactory response to cessation of alcohol consumption.—I am, etc.,

J. SHAFAR.

Burnley General Hospital,
Burnley, Lancs.

Menstrual Red Eye

SIR,—The correspondence on this subject initiated by Mr. M. D. O'Brien (February 4, p. 359) and continued in your issue of February 25 (p. 589) is of particular interest to me for two reasons. Last month I met a Javanese lady from Sarawak on a German ship who developed extensive bilateral conjunctival haemorrhages the day before a menstrual period. She had experienced similar " mata mera " (red eyes) on one side only before each of her two previous menstruations, and had noticed increasing menorrhagia. Her Hess's test was strongly positive, and at my suggestion the ship doctor gave her oestrogen therapy. The Hess's test was normal after 24 hours' treatment.

I have previously described a haemorrhagic diathesis due to increased capillary fragility and mentioned other descriptions of premenstrual thrombocytopenia and purpuras in women, associated with increased capillary fragility.[1] In the last four years, using a standardized capillary resistance test in Singapore (Hess's test with cuff at 80 mm. Hg for 10 minutes) I have found that capillary fragility in women usually increases in the 10–14 days prior to menstruation and reaches a maximum round about the first day of menstruation. There are considerable individual variations in maximum fragilities, but European women tend to have higher capillary fragilities than Chinese or Malay women, and a tendency to easy bruising is not uncommon among European women in the immediate premenstrual period or during the menopause. At both these times the blood oestrogen levels tend to be relatively low. The administration of small dosages of oestrogens to women with increased capillary fragility during the premenstrual period or menopause has been found to reduce the capillary fragility to normal levels within 24 hours and seems to reduce any associated tendency to easy bruising. Glucocorticoid therapy is not similarly effective. All this strongly suggests that in some women physiological falls in blood oestrogen levels may result in a haemorrhagic tendency due to increased capillary fragility. I suspect this is the mechanism behind " menstrual red eye."—I am, etc.,

RONALD WELLS.

Saffron Walden, Essex.

REFERENCE

[1] Wells, R., *Lancet*, 1958, 1, 886.

SIR,—Mr. M. D. O'Brien's letter (February 4, p. 359) and the subsequent interesting correspondence on eye disorders associated with the menstrual cycle illustrate some few of the many ocular disturbances due to or affected by the menstrual cycle.

Yet another condition is manifested in a 41-year-old woman presently attending this hospital. When she was first seen she described " matter inside the left eye " which appeared and disappeared regularly. Although the eye was normal at this visit, she was subsequently found to have hypopyon iritis which recurs with the menstrual periods, regular or irregular, and according to the patient's description this has been happening for over three years. The pus forms usually just before the start of the period and disappears after two days to leave a relatively quiet eye. The only source of focal sepsis which could be found was a chronic cervicitis which was adequately treated, but despite this the condition persists.

Investigations are being made into this and similar cases, but so far the immediate cause of the iritis has not been detected—culture of the blood and anterior chamber have been sterile and no hormonal disturbance has been found. A marked eosinophilia does, however, suggest an allergic cause. In the meantime, despite the quiet state of the eye between attacks, signs of damage are accumulating, and unless the enigma is solved quickly the condition will probably be stopped by artificial (radium) menopause.—I am, etc.,

J. STANLEY CANT.

Southern General Hospital,
Glasgow.

Leukaemia Cases with Previous Radiotherapy

SIR,—Several months ago you were good enough to publish a letter (June 11, 1960, p. 1810) in which we asked for the opportunity of studying the chromosomes of blood and bone marrow cells of mongols with leukaemia. In consequence of the publication of that letter, and a similar letter in the *Lancet*, we were able within a few months to study five such cases as well as the first known instance of the occurrence of mongolism and leukaemia in one sibship. The results of these studies have now been published.[1 2] We are encouraged by the success of our previous appeal to ask again for the opportunity to carry out chromosome studies in certain cases of leukaemia.

We have just prepared for publication an interim report of the results of our chromosome studies in acute leukaemia,[3] other than acute leukaemia in association with mongolism. Of 22 cases of acute leukaemia in adults, seven gave a history of having had radiotherapy for some disease other than leukaemia within the preceding 12 years. In these seven cases we believe there is an increased possibility that leukaemia was radiation-induced.[4] Definite chromosome abnormalities were found in five of these seven cases. In contrast, abnormalities were demonstrable in three of 15 cases without a history of previous radiotherapy. Cases of leukaemia with such a history of radiotherapy are probably uncommon, but we feel that their investigation may materially help us in the elucidation of the leukaemogenic risk of radiation exposure. Accordingly we would be grateful for the opportunity of studying such cases before the instigation of treatment for the leukaemic condition. As there is no evidence relating radiation exposure to chronic lymphatic leukaemia, the cases in which we are interested are those of acute leukaemia and chronic myeloid leukaemia with a significant exposure history. For this purpose significant exposure history means having received a therapeutic dose of a radio-isotope or treatment with either *x*-rays or radium to any part of the trunk, other than for skin diseases, at any time during the 12 years prior to the diagnosis of leukaemia.

The blood and bone-marrow samples we require are taken in the usual way, and this can be done at the same time as samples are taken for diagnostic purposes. Although materials for chromosome studies require special handling immediately after they are taken, we would be glad of the opportunity of studying anywhere in Britain cases of leukaemia which may be radiation-induced.—We are, etc.,

M.R.C. Clinical Effects of Radiation Research Unit, Western General Hospital, Crewe Road, Edinburgh 4.

A. G. BAIKIE.
W. M. COURT BROWN.
PATRICIA A. JACOBS.

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2. Tough, I. M., Court Brown, W. M., Baikie, A. G., Buckton, K. E., Harnden, D. G., Jacobs, P. A., King, M. J., and McBride, J. A., *Lancet*, 1961, 1, 411.
3. Baikie, A. G., Jacobs, P. A., McBride, J. A., and Tough, I. M., in preparation.
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"Les Manipulations Vertébrales"

SIR,—In the *B.M.J.* of December 31, 1960 (p. 1939), Dr. James Cyriax reviewed my book *Les Manipulations Vertébrales*. So far all the reviews that I have received from France and abroad have been very favourable indeed. It is only fair that some reviews should be less favourable. But if I feel that some of the reviewers who have praised my book have hardly read it, I am certain that Dr. Cyriax has read it very badly or else that he has not understood it.

This is why I wish to explain in your columns for the benefit of all those (and there will, no doubt, be many) who will never read it, but who might have read Dr. Cyriax's review, that the aim of the book is: (1) to offer a rational method of the application of vertebral manipulations based on an objective clinical examination; (2) to describe the indications, contraindications, and complications of these treatments; (3) to study the different modes of action of the manipulations; and (4) to clarify and describe all useful and available techniques.

Therefore, the aim of this book is to show that manipulation is an interesting form of treatment which has its place in traditional medicine. The book is intended for physicians and not for physiotherapists. It is certainly a very long way from the osteopathic theories of A. T. Still, but it is not very near those of Dr. Cyriax. I hope he will forgive me.—I am, etc.,

Paris. R. MAIGNE.

Marking the Skin

SIR,—An efficient skin-marking ink is a valuable asset in certain surgical procedures, especially in the surgery of varicose veins, since in these cases it is usually necessary to mark every branch prior to operation.

For many years I have found this to be a difficult problem, since all the inks I have used have had varied deficiencies. The ideal ink dries immediately, is non-toxic to the skin, and is not removed by the fluids used in pre-operative preparation. It should also be cleanly and easily applied. I have found that the pen with a felt nib known commercially as the "Speedry Magic Marker" fills most of these requirements. Although hard rubbing with spirit will remove the ink, it remains stable provided pre-operative applications are made carefully. This product is used extensively in industry, but I now call attention to its surgical use.—I am, etc.,

London W.1. R. ROWDEN FOOTE.

Pressure-cooker Sterilization

SIR,—It has been my practice in cases of tonsillitis, mumps, scarlatina, etc., to advise patients in the interest of hygiene to put all crockery and cutlery used by the patient into a bucket or bowl and pour on "dettol" or some such disinfectant, then a kettle full of boiling water and leave to cool, and finally to wash the articles in the usual way.

I was giving these instructions to a patient a few days ago, when she interrupted and said, "Oh doctor, I boil them up in the pressure cooker for 15 minutes." In these days, when pressure cookers are fairly common, surely this is a first-class idea well worth passing on.—I am, etc.,

Cheam, Surrey. W. LAWSON.

POINTS FROM LETTERS

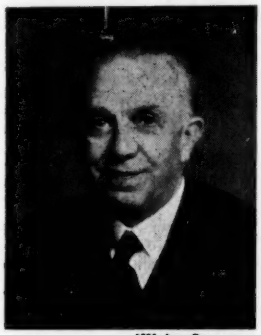
Prescribing Costs

Dr. DENIS TRIMBLE (Birmingham) writes: One of my patients has just reported for re-dressing following an accident and treatment at hospital. On his left leg was a full-length 6-in. (15-cm.) crepe bandage, under which was a 2-in. (5-cm.) superficial abrasion. And it's the G.P.s that are blamed for excessive prescribing!

Obituary

Lord STOPFORD, K.B.E., M.D., Sc.D., LL.D. F.R.C.P., Hon.F.R.C.S., F.R.S.

Lord Stopford of Fallowfield, who died at his home at Arnside, Westmorland, on March 6 at the age of 72, was one of the first 14 people to be granted a life peerage. His career demonstrated that the man of learning at all events does not share the supposed misfortune of the prophet. A Lancastrian born and bred, he entered Manchester University at the age of 18, and during an unbroken association rose through successive offices to be its professor of anatomy at 30 and its vice-chancellor at 46. Later he became professor of experimental neurology. It was for his original work on sensory pathways and on the blood supply of the brain that he was elected F.R.S. in 1927.



[*Walter Stoneman*

John Sebastian Bach Stopford was born on June 25, 1888, at Hindley Green, near Wigan, fewer than 20 miles from the university at which he rose to eminence. From Manchester Grammar School he entered the university as a medical student in 1906. He gained many prizes during his student career, among them the Bradley memorial scholarship in clinical surgery, the Dumville surgery prize, and medals in anatomy, histology, and pathology. He graduated in medicine and surgery with second-class honours in 1911. After holding resident posts in the Royal Infirmary and the Rochdale Infirmary he joined the staff of the university in 1912 as a junior demonstrator in anatomy, becoming a senior demonstrator a year later, and lecturer in anatomy in 1915, in which year he proceeded M.D. with gold medal. It was in this department that he met his future wife, Miss Lily Allan, herself a medical graduate of Manchester University, a demonstrator in anatomy, and an ophthalmic surgeon. They were married in 1916, and had one son.

In 1919, on the resignation of the late Sir Grafton Elliot Smith, Stopford succeeded to the chair of anatomy, an appointment extremely popular among the students. As professor he maintained the school of neurological anatomy which Elliot Smith had founded in Manchester. His own experience in the first world war had intensified a previous interest in neurology and particularly in the anatomical basis of sensation. He was neurologist to the Second Western General Hospital and afterwards to the Grangethorpe Hospital, where he not only rendered valuable help in the treatment of the large number of cases of nerve injury which were received, but elucidated much concerning the mode of distribution of the sensory nerves.

In his work in his department Stopford set himself the tack of differentiating all the various elements concerned in sensation. Papers on the subject by him are to be found in *Brain* and other journals of this period, and his work was recognized in 1927 by his election to the Fellowship of the Royal Society. His book, *Sensation and the Sensory Pathway*, published in 1930, was a most valuable contribution to this subject, confirming most of Head's observations, and carrying them further in some directions. Apart from the value of the original work which the book embodied, it exemplified Stopford's skill and lucidity in presentation. He was equally gifted as an expositor and as a researcher. Later he devoted himself, with Professor E. D. Telford, the holder of the chair of systematic surgery at Manchester, to study of the nerve supply of the blood vessels and the treatment of certain arterial diseases. A year or two after he became Vice-Chancellor of the University he gave up the professorship of anatomy, in which he was succeeded by Dr. Wood Jones, and himself became professor of experimental neurology. He also acted as honorary advisory anatomist to Manchester Royal Infirmary.

While carrying out all this engrossing work in his department, he became more and more absorbed in the affairs of the university as a whole. He furnishes another of those many instances in which anatomists, for some reason, have shown exceptional skill in administration either in academic affairs or in offices of state. Over a period of six years, broken into two periods, he was dean of the medical school; he was also chairman of the Board of Medicine, and for several years he represented the Senate on the University Council. In 1928 he was made Pro-Vice-Chancellor, and in 1935 he was appointed, amid universal approval, Vice-Chancellor in succession to Sir Walter Moberly, who had held the office since 1926. It was felt to be peculiarly fitting that a Manchester undergraduate who had given such proof of his devotion to his university should become its academic head. "It is a joy for me to work in this place," he said on his election, "and I can assure you it is easy for me to give of my best. I am only afraid that my best may not be good enough." The late Sir Geoffrey Jefferson wrote that though Manchester University gained a remarkable Vice-Chancellor it lost an anatomist and original research worker of great achievement and still of great promise when he made the change . . . in response to his sense of public duty. Stopford loved and believed in the university. His interest in it was general and not confined to his own department. In all his university offices he showed great administrative ability and a sympathetic understanding of the difficulties of his colleagues in all the faculties. He was wise and far-seeing, able to get quickly at the heart of a problem, and with a genius for enlisting general good will. He retired from the office of Vice-Chancellor in September, 1956, after 21 years of devoted service to his university. In the following month the freedom of the City of Manchester was conferred upon him.

As Vice-Chancellor he entered upon many important tasks. One of these was the completion of the great new library of 300,000 volumes, leaving the famous Christie library as a science collection. Another was the establishment of Lister House, a hall of residence at which every medical student spends three months in the later part of his course. In 1927 he was appointed the representative of the Manchester Medical School on the General Medical Council. Here also his qualities were quickly appreciated, especially on the educational and examinational side of the Council's work. In 1939, on the death of Sir Robert Bolam, he was made its Chairman of Business, a position second in importance only to that of the President.

Outside his university, he also gave good service to the cause of education. Indeed, education in all its aspects interested him. He was chairman of Ladybarn School, a governor of Manchester High School for Girls and of Withington Girls' School, and a member of the Manchester Education Committee. He was chairman of the council of John Rylands Library, and—an appropriate office for one named after the great German composer—chairman of the Manchester College of Music. Another office was that of chairman of council of the Universities Bureau of the British Empire. His interest in student welfare was unflagging. For many years he was honorary treasurer of the Women's Athletic Union at Manchester. He was himself in earlier years a football enthusiast, and in later life often a spectator at matches, but the recreation he loved most at his home at Rusholme was gardening.

In 1941 he became Sir John Stopford. The honorary degrees of Doctor of Science of the sister universities of Dublin, Leeds, and Cambridge were conferred on him. He was elected F.R.C.P. in 1942 and honorary F.R.C.S. in 1955, and in 1953, when the University celebrated its jubilee, Liverpool conferred on him the honorary degree of LL.D.

He received the honorary degree of D.C.L. from Durham University in 1957. He had been president of the Manchester Medical Society, vice-president of the Anatomical Society of Great Britain and Ireland, vice-chairman of the Interdepartmental (Goodenough) Committee on Medical Schools, vice-chairman of the managing trustees of the Nuffield Foundation, and a member of the medical advisory committee of the University Grants Committee. For many years before the National Health Service came into being he was chairman of the Manchester, Salford, and Stretford Joint Hospitals Board, and consequently he was the obvious choice for the chairmanship of the Manchester Regional Hospital Board. The life peerage conferred on him in 1958 was some recognition of his remarkable services to Manchester, to medicine, and to higher education.

When he retired from the Vice-Chancellorship in 1956, Manchester University recorded its admiration and gratitude at a dinner given to him and Lady Stopford. In his tribute to them, Lord Woolton, the Chancellor of the University, said on that occasion: "The simple secret of their lives is that they are good people and uncompromising servants of their own standards of integrity."

Sir HARRY PLATT, Bt., writes: Although John Stopford attained to the highest academic distinction, as an undergraduate and later as a medical scientist, he was in many respects the antithesis of the intellectual—if indeed the intellectual be an easily recognizable type of human. His outstanding attribute was common sense, elevated in him to the pinnacle of genius. It was this quality above all which gained for him an unrivalled reputation as a leader—as a vice-chancellor, as vice-chairman of the Nuffield Foundation, and as the first chairman of the Manchester Regional Hospital Board—to name only three of the offices in which he has left behind indelible impressions of his manifold talents.

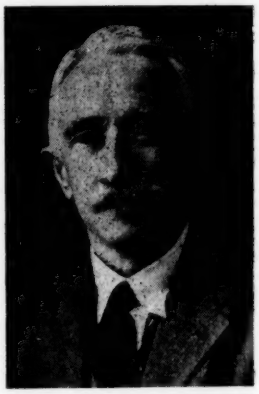
Looking back over the long years of my close association with him, I fail to remember what in the end persuaded him to stay with anatomy. It was perhaps the magic of Elliot Smith. For Stopford possessed great manual dexterity, and he would have made a most successful surgeon, a field to which he was first attracted. It is not easy—probably impossible—so soon after his death, to single out any one of his contributions which could be regarded as his supreme monument. His position in the university world—that goes without saying. But I venture to predict that the achievement which will have as lasting an influence as any other was the prestige he gave to the Manchester Regional Hospital Board in its early formative years. He laboured unceasingly to spread the standards of university medicine throughout the region. At this time, we who were his colleagues felt that, although he was driving himself far too hard, he relished the burden of this new mission which had been laid upon him. He was a man completely unspoilt by the honours which came to him; and he remained to the end of his days the sterling, sturdy Lancastrian personality who was a friend to all sorts and conditions of men.

W. G. GRANT, M.D., F.R.C.O.G.

Professor W. G. Grant, emeritus professor of obstetrics and Gynaecology, University of the Witwatersrand, died in Natal, Union of South Africa, on November 15, 1960, at the age of 87. He had for many years been the doyen of South African gynaecologists, although he had retired from practice in 1945.

William Gordon Grant was born at Glenlivet, Banffshire, Scotland, on May 15, 1873. He was educated at Tombai and Chapeltown Schools, and then went to Drainie, where he was taught by Mr. Ramsay Macdonald. On leaving Elgin Academy he entered the University of Aberdeen, from which he graduated M.B., C.M., with honours, in 1895. He won the Shepherd medal for surgery, and on being awarded the Thompson travelling fellowship he went to Germany, where he worked under Virchow, Olshausen, Wieber, and Martin. At Munich he worked in von Winckel's gynaecological clinic. Returning from the Continent he worked at the Chelsea Hospital for Women, but later left for Paris, where he held appointments in several hospitals.

Gordon Grant was a good linguist, becoming proficient in German and French during his student days, and also acquiring a working knowledge of Yiddish and Afrikaans. He also learnt Arabic when he went to Northern Nigeria in 1900 as a medical officer serving with an expeditionary force. He saw action in the field at this time and appears to have been among the first white men to have set eyes on Lake Chad. He maintained his interest in Arabic, and in later years frequently read works written in Arabic script.



In 1904 he came to Johannesburg and was appointed gynaecologist to the Johannesburgh General Hospital and to the Queen Victoria Maternity Hospital. He later became professor of obstetrics and gynaecology at the University of the Witwatersrand and held that post until 1938, when he retired on reaching the age limit. He was elected F.R.C.O.G. in 1929. During the first world war he served as a major in the South African Medical Corps. He was a member of the B.M.A. for over 60 years and served on the Witwatersrand Branch Council for several years.

A colleague writes from the University of the Witwatersrand: Gordon Grant was a great personality and a strong man. Subordinate staff often feared him, but many of us held him in the greatest affection. He was a man of steel, erect in carriage, slim, and in good health until very recently. A man of such intellect and ability was a valued asset to a young medical school, and, in fact, to a young community, and his insight and wisdom led to invaluable advice on many occasions. He was a natural clinician and used his wide experience profitably. A man like Gordon Grant simply had to be a highly competent and fearless surgeon. South Africa is proud of this great man, and he will live long in the memory of this university and this virile community on the heights of the Witwatersrand.

D. E. DERRY, *M.C.*, M.B., Ch.B., Hon.F.R.C.S.

Professor D. E. Derry, formerly professor of anatomy at the Egyptian University, Cairo, and an expert Egyptologist, died suddenly at his home near Saffron Walden on February 20. He was 86 years of age.

Douglas Derry was born on November 1, 1874, and graduated M.B., Ch.B. at the University of Edinburgh in 1903. Thereafter he held the Crichton research scholarship in anatomy at Edinburgh and then became demonstrator of anatomy there. Not long afterwards he went to Cairo as assistant to the professor of anatomy at the Government School of Medicine, and there he soon interested himself in archaeology and anthropology, besides contributing many papers on anatomical subjects to the *Journal of Anatomy and Physiology* and other journals. He was anthropologist to the Archaeological Survey of Nubia, and wrote an interesting account of his work during this survey. For a time he was lecturer in physical anthropology and curator of the anatomical museum at University College.

During the first world war he served as a captain in the R.A.M.C., and was awarded the Military Cross. Soon afterwards he became professor of anatomy in Cairo and remained there until he was evicted from his chair, like the rest of his British colleagues. In his later years in

Egypt he wrote several papers on mummification and on other archaeological subjects. He was elected an Honorary Fellow of the Royal College of Surgeons of England in 1949.

Professor R. WHEELER HAINES writes from Bagdad: In 1947 when I first met him Derry was already an institution, for he had been in Egypt so long he had taught all the practising doctors trained in the country and quite a few retired ones. Everyone asked, "Do you know Derry?" as a sort of test of social acceptability. It was a good test because of his very high standard of hospitality. As a teacher Derry had his difficulties—mainly the great numbers of students and a scarcity of bodies. For my 100 students of a new school he explained he could only spare three bodies—it was the best he could do, and a fair division. However, the cholera epidemic solved that shortage, at least temporarily, and he carried on lecturing in his enormous theatre, often to more than 1,000 students at once, while I took my 100 in one of his annexes, for the College I had come to work in was not actually built till later. His theatre had large accessible windows, so students climbed in and out all the time. Often they brought newspapers and discussed politics quietly as the lecture proceeded.

We were both troubled by thefts of bodies from the dissecting-room, and Derry followed up some of his losses. He ran one leg to earth under a student's bed, wrapped up in newspaper: in the evenings it went on the bed, with the newspaper spread out, for anatomical study. Some students Derry rather admired had stolen a complete corpse, dressed it and driven it sitting up in the back of an open car, talking to it as they passed the police guards.

The days he liked to remember were those of the Tutankhamen discoveries, when he unwrapped the king's mummy. But most of his colleagues, the archeologists, were already dead—killed, so many people believed, by the ancient curse inscribed on the tomb door. It didn't work on Derry. There was once a surge of indignant police (the students had killed their leader with a bomb thrown from the roof of the College into the street below, and followed it up by bottles of concentrated acid from the chemistry lab), who swept through the building, beating up everybody they found, killing two farrashin and mauling the professor of physiology, but they missed Derry, who was quietly sitting in his room. This was the occasion on which his dissecting-room attendant, who looked like a corpse himself, stripped off his overall and galabiyah and laid himself out naked on a dissecting-table to escape the rioters. On the day a student brought a loaded automatic to the anatomy oral examination he shot me, but the shell meant for Derry jammed between the magazine and breech. So Derry (then in his 70's), who had slipped in an attempt to attack the assailant, only got a beating on the head with the butt, bloody but ineffective, till he was rescued by his senior assistant, now his successor in the chair. He drove himself to the hospital. After that King Farouk decorated us both with the order of El Ma'arif, 2nd class, with a citation for long service (40-odd years in his case, 3 in mine), but this was, of course, cancelled at the revolution.

Some of his character got through to his assistants. This was important in Egypt at this time, when bribery, often paid in rare postage stamps, was a recognized aid to passing examinations. Derry's men were hard-working and unbribable, which could not be said of some of the other professors' assistants. When Derry left he went alone, with no one to see him off or mention his great services to Egypt. But the men he taught, largely by stories of his early experiences as a doctor, stories the students knew by heart and loved, got something from him. We have few such teachers nowadays.

Professor LAMBERT ROGERS writes: Professor Douglas Derry was one of a small group of anatomists which included Thomas Yeates, the late John Kirk, A. J. E. Cave, and P. K. Chanmugam, of Ceylon, whom the Council of the Royal College of Surgeons has honoured by electing to the Fellowship of the College. His death takes from us not only a distinguished anatomist and Egyptologist but a man of charm and vision who was also a delightful host, guide, and companion to those of his friends who visited him in Egypt. To go round the Cairo museum and the ancient tombs at Sakara with him was an experience which anyone who had this pleasure will long remember. While professor of anatomy in Cairo he became a well-recognized authority on ancient Egypt, and it was he who, when the mummy of Tutankhamen was discovered, unwrapped it and reported on the body of the king. Those of us who in 1947 were in Cairo examining for the primary fellowship examination will recall his care for us, and his courtesy and kindness in making our visit a truly memorable one.

G. F. MANZOCCHI, M.D.

Dr. G. F. Manzocchi, who was in general practice in the West End of London, died suddenly on February 2 at the age of 56.

Gerolamo Filippo Manzocchi was born in Morbegno, Sondrio, in Northern Italy, on April 18, 1904. He started his medical studies at the University of Pavia and then went on to Milan University, where he worked under Professor Carlo Besta at the Institute of Neurology, graduating M.D. with a thesis on haematomyelia in 1928. He went into practice in the small Alpine mountain town of Valmasino. Coming to London in 1930, he was resident medical officer at the Italian Hospital for four years, and then entered private practice in the West End of London, where he gradually built up a successful practice which included a large number of Continental patients.

Although his sympathies were not with the Fascist régime he was interned in June, 1940, when Italy entered the second world war. He survived the tragic *Arandora Star* disaster and was soon afterwards sent to Australia, where he was released from internment in 1943 and subsequently became resident medical officer in a sanatorium in the vicinity of Melbourne. In 1945 he returned to London and within a short time built up an extensive practice. Because of his past associations with the Italian Hospital he played an important part in restarting activities there which had been suspended during the war years, and he was subsequently appointed honorary physician to out-patients, a position he held up to the time of his death. In addition to his busy practice he was physician to several Italian shipping companies and to Air Italia, and he attended medical boards at the Italian Consulate in London. In his student days he represented Italy at basketball and his universities at association football, and in the early twenties he did some motor racing on the Monza track; throughout his life he remained an excellent and keen motorist.

The personality, charm, and vitality of Dr. Manzocchi endeared him to innumerable patients of many nationalities and in many walks of life. He was bilingual in English and Italian and also spoke fluent French and Spanish. A very good clinician, with an alert, well-informed intellect, he possessed a truly cultured background. His many acts of kindness, generosity, and common sense made his patients turn to him for advice and support. He was a witty man with a direct manner which he would never hesitate to use to debunk anyone or anything which to him appeared mean or petty. His main interests were his practice, which often took him all over Greater London; his happy family life; and his considerable knowledge of food and wines, in which he was a true gourmet. In recent years, in spite of failing health, he continued his work in top gear without relenting, and he died suddenly as he would have wished whilst in full harness. We have lost an outstanding personality and doctor and a very loyal colleague and friend. Our deep sympathy goes to his widow and son.—J. B. V.

E. M. writes: With the sudden death of Dr. G. F. Manzocchi the medical world of London's West End has lost a well-known and well-loved figure. He will be particularly missed at the Italian Hospital, where he held a weekly out-patient session on Saturday mornings. This was attended particularly by Italians resident in outlying

districts, especially in Bedford, who found it convenient to attend hospital on their day off work. To them he would bring not only the benefit of his sharp clinical sense and the true compassion of a born doctor, but also the comfort of fellow feeling and of an optimistic nature overflowing with vitality. We as colleagues at the hospital had learned to respect his opinion both in professional matters and in matters of policy regarding the hospital within the medical committee. Dr. Manzocchi was well known to a large number of leading consultants in London, as, excellent physician that he was, he was never slow to seek further advice whenever this seemed to be in the interests of his patients. His last few years were punctuated by repeated attacks of the illness that was to kill him, and, although he had full knowledge of the possible consequences, it was difficult for his medical advisers to hold him back from work for more than the bare minimum and to quench his zest for life. This was in fact his outstanding characteristic and it endeared him to all who came in contact with him.

G. J. HARRISON, L.R.C.P.&S.I., D.P.M.

Dr. Geoffrey John Harrison, medical superintendent of Winwick Hospital, near Warrington, died on January 31. He was 54 years of age.

Geoffrey John Harrison was born in Dublin on May 13, 1906. Educated at Mountjoy School, he studied medicine in Dublin, qualifying in 1929. After holding the post of assistant medical officer at St. Patrick's Hospital, Dublin, he took the D.P.M. and joined the staff of Winwick Hospital, where he remained up to the war years, when he served in the R.A.M.C., attaining the rank of major and being mentioned in dispatches for distinguished service. His health was seriously affected by his war service, but he continued his psychiatric work at Rainhill Hospital and Prestwich Hospital before returning to Winwick in 1948 as deputy medical superintendent. He was appointed medical superintendent in 1953.

During his early days Dr. Harrison was a keen and knowledgeable sportsman, captaining the Winwick Hospital staff cricket team from 1934 to the outbreak of war. He was a sound and capable administrator of absolute integrity, held in high regard by his colleagues and well beloved by his patients, whom he served to the best of his ability. "Geoff" was a friendly, hospitable, and unassuming man who showed a broad humanity from which an easy charm and kindness flowed readily. His later years were marred by continuing ill-health, borne with exemplary fortitude. He will be missed by many, and deep sympathy goes to his widow and son in their sad loss.

R. K. A. VAN SOMEREN, F.R.C.S.Ed.

Mr. Richard Kenneth Alexander van Someren, who practised as a surgeon in Nairobi and was surgeon to the Mount Kenya Hospital, Nyeri, died in Edinburgh on February 8, 1961, aged 47.

C. V. T. writes: The death of Ken van Someren has caused universal distress in Kenya. Beloved as he was by all those who knew him, I have personal and special reasons for saying that his death has robbed not only the medical fraternity but the whole of Kenya of a personality fragrant with love for his fellow men and women. Born on April 28, 1913, in Jinja, Uganda, where his father was Government medical officer, he was sent at the age of 5 to be educated in Edinburgh, where he qualified in 1935, taking the Fellowship of the Royal College of Surgeons of Edinburgh in 1938. Joining the R.A.M.C., he saw active service in the Norwegian campaign in the second world war, and subsequently ended up as a lieutenant-colonel on the Burmese front. Here he contracted scrub typhus, which was at that time considered to be a most virulent and incurable disease. He returned to his beloved Kenya in 1945 and entered Government service, but transferred to a private medical firm in Nairobi in 1950. It is difficult to express our sorrow by mere words, but we can at least extend our sincere sympathy to his dear wife, his family, and his relatives; we can and do assure them that Ken's memory will be engraved upon our hearts.

Sir THOMAS FAIRBANK, D.S.O., O.B.E., M.S. F.R.C.S.

The obituary of Sir Thomas Fairbank was published in the *Journal* of March 11 (p. 751).

H. J. S. writes: Sir Thomas Fairbank held a unique place in British orthopaedics. Like Sir Gordon Gordon-Taylor he belonged to a generation distinguished for its dignity and urbanity. No man could have been more friendly, but without displaying or encouraging familiarity; he inspired respect as well as affection. Although a quiet man, averse from pontificating, his opinions were firmly held and his conduct marked by Roman rectitude. Without being conscious of it he was a great pioneer, and this was the result of one thing, being supremely good at his job and retaining into his last years the enthusiasm of a schoolboy. At King's College Hospital, at Great Ormond Street, and at Alton orthopaedics flourished simply because he was there.

No one could have been more unpretentious. Fairbank made no claim to be a scientist. His intense interest in generalized diseases of bone was that of a collector rather than an investigator. He was consulted by his colleagues and juniors all over the country. Taking case notes and *x* rays to him for an opinion was like visiting a keen numismatist. He seized on to them, studied the notes, compared the *x* rays with others in his remarkable collection, then gave his opinion firmly though not dogmatically. And often, in conclusion, he would ask if he might have copies of the data—an addition to the collection, another piece of knowledge. He was a clinician with unusual powers of observation and the ability to record facts with great precision. This was the basis of his ideas, with the result that nothing he wrote has ever had to be questioned.

A great, wise, and lovable man has come to his journey's end. In remembering Thomas Fairbank we may echo the words that Longfellow wrote of a friend:

> "Of all the many lives that I have known
> None I remember more serene and sweet,
> More rounded in itself and more complete."

Dr. C. S. P. HAMILTON writes: As an old Charing Cross student I feel it encumbent on me to add to the obituary notice on my old chief. A great deal has been written concerning his brilliant career, but not very much about his military service. Well do I remember a dark, dismal, rainy night in the Ypres salient, in September, 1915. My R.A.P. was in the cellar of "Château Rosenthal," the floor covered with stinking blood and mud-soaked straw; only a glimmer of light was allowed, since the post was in observation line of the enemy. A big and swearing sergeant-major was brought in suffering from a G.S.W. of the thigh. I was in a devil of a fix—the room was full of wounded. Suddenly the field ambulance bearers arrived, and who should be in charge but Captain Fairbank. Never was a young regimental medical officer more relieved and pleased, for Fairbank was his old teacher and revered chief. I remember the care he took in setting the fracture and dressing the wound, how quiet he was and cheerful when we were all depressed. It was a night of heavy shelling around our post, but "Tommy F" was so calm, and as brave as a lion. In Salonika he took over the appointment of transport officer in charge of mules—this caused great amusement to the medical officers of the division, but he seemed pleased with his new assignment and not in the slightest cognizant of the extraordinary situation—a well-known surgeon in charge of mules. He was always cheerful and cheered us all. Later he took over his rightful position as consulting surgeon. Unfortunately he fell a victim to a serious malarial infection which incapacitated him for some time: it is possible his deafness may have been due to that severe malarial attack. God rest the soul of that great surgeon: a more humble and kindly man could seldom be found.

L. C. D. HERMITTE, M.B., Ch.B., D.T.M.&H.

The obituary of Dr. L. C. D. Hermitte was published in the *Journal* of February 18 (p. 508).

A. R. writes: While a student at Edinburgh University Hermitte became greatly interested in pathology as a subject, thanks largely to the teaching of Professor J. Lorrain Smith, whose method laid emphasis on the need for correlating all aspects of a case—the macroscopic and microscopic together with the clinical. This undoubtedly influenced his choice of a career, and, had circumstances permitted, he would have taken up this line of work, clinical pathology, at a much earlier date. His enthusiasm for his subject was boundless, and this was reflected in his keenness as a teacher. He went to great pains to ensure that his lectures were clear and up to date, and he never tired of stressing the fact that the basis of clinical medicine should be a sound knowledge of pathology, which, he emphasized, must not be regarded as an end-product but as a continuous process occurring in the living subject. His early retirement meant the loss of a zealous worker and a fine teacher.

Medical Notes in Parliament

BRINGING SOCIAL HELP TO THE WOULD-BE SUICIDE

[FROM OUR PARLIAMENTARY CORRESPONDENT]

The Suicide Bill seems likely to go through the House of Lords without alteration. Certainly those amendments proposed for the committee stage on March 9 were all withdrawn, although a second look may be taken at one or two of them.

The point of principal interest arose in a general discussion on Clause 1, which declares simply and shortly that "The rule of law whereby it is a crime for a person to commit suicide is hereby abrogated." With this goes the abolition of the offence of attempted suicide. Lord SILKIN drew attention to the fact that suicide would still remain a social problem. There were tens of thousands of attempts at suicide every year, all of them meaning that some person had been driven to the point of desperation. He pleaded that in some way it should be ensured that every person who had attempted suicide should be seen by someone—psychiatrist, mental welfare worker, church worker—and given help. Punishment and imprisonment were not the right form of treatment, but some form of treatment was necessary in most cases. Lord TAYLOR thought that it was the ordinary members of the public who required guidance—the relative or friend or whoever it might be who discovered that somebody had attempted to commit suicide and had to decide what to do.

The LORD CHANCELLOR recalled that in the second reading debate the Bishop of Carlisle had wanted to have the wrongfulness of attempted suicide underlined. He thought that the Bishop had in mind some compulsory power on the lines of those in the Mental Health Act, Part IV. After consultation with the Minister of Health he had reached the conclusion that this would not be practicable. Most persons who attempted suicide would receive treatment, either because physical injury necessitated admission to hospital, or because their mental condition was such that the powers in the Mental Health Act were applicable. In the former case the Minister of Health was making arrangements to ensure that the need for psychiatric treatment would be considered. There would be few cases in which a person attempting suicide would not receive, either voluntarily or under compulsion, the care and treatment needed. An express provision in this Bill extending compulsory powers to this small number of cases would have to be drafted so that it would apply to every person who attempted to take his own life; there was nothing in the nature of the attempts to distinguish the small minority. Such a provision would be open to serious objection. It would mean in effect that the fact that a person had attempted suicide should be evidence of mental disorder. It was not true of some of these persons that they were suffering from mental illness, and there was to him a great difficulty in subjecting such a person to treatment designed for those who were mentally ill.

QUESTIONS IN THE COMMONS

Items Costing Less Than 2s.

Mr. A. E. ORAM (East Ham, South, Lab.) asked the Minister of Health on March 6 what steps he proposed to ensure that a patient was not required to pay 2s. for an item prescribed under the Health Service for which the ordinary retail price was less than 2s. Mr. ENOCH POWELL said that he expected the chemist to sell such items at the retail price. Guidance had already been given to chemists by their professional organization, and he was considering with them what further guidance, if any, was needed. There would be only a very small percentage of items in prescriptions of which the retail price was under 2s., he added.

Mr. K. ROBINSON.—Is the Minister saying that the chemist is entitled to alter a doctor's prescription, and to strike off an item if he can supply it over the counter if it costs less than 2s.? Hitherto a number of chemists have been under the impression that in no circumstances are they allowed to alter a doctor's prescription. Mr. POWELL.—Yes. The item is marked "Not dispensed," and the prescription form so marked is returned to the executive council.

Medico-Legal

NEGLIGENT PSYCHIATRIC TREATMENT

[FROM OUR LEGAL CORRESPONDENT]

In an action in the High Court, Mr. Justice Barry on March 7 awarded damages of £6,000 against Dr. Theodor Alfons Werner, of Wimpole Street, for negligence in psychiatric treatment given to his patient, Miss Alice Landau, of Talbot Road, Highgate. In his judgment, Mr. Justice Barry expressly acquitted Dr. Werner of the accusations of professional misconduct which had been made against him. (*The Times*, March 8.)

Cause of Action

The cause of action in this case is interesting and (it would seem) novel. It was alleged that by his social conduct outside the consulting-room Dr. Werner had injured his patient. Counsel for the plaintiff founded his case on the proposition that, if one were treating a person in the psychotherapeutic sense, all conduct formed part of the treatment, whether it was inside or outside the consulting-room.

Between March, 1949, and August, 1949, Dr. Werner treated Miss Landau by a system known as transference. By May 28, 1949, Miss Landau was emotionally aroused towards Dr. Werner by the treatment. Dr. Werner advised her to go on with the treatment, telling her that the feeling of obsession, love, and bondage would cease. By the end of this treatment Miss Landau was very much in love with Dr. Werner, but was very much better in health, though not wholly cured. Up to this point, held Mr. Justice Barry, the treatment was entirely proper. At this stage Dr. Werner feared that Miss Landau might, if she was removed from his influence, have a relapse into her former anxiety neurosis. He could have ceased contact with Miss Landau in August, 1949, but instead he decided to guard against a relapse by continuing to have a series of social contacts with Miss Landau. Those contacts did occur, but Mr. Justice Barry held that the improper incidents which allegedly took place were simply delusions on her part. The result of these contacts, however, was a severe mental

disturbance culminating in a suicide attempt. It was on this series of social contacts that the finding of negligence was based. No blame attached to Dr. Werner for his later contact with Miss Landau when in 1951 he attempted to resolve the transference at the request of another doctor.

Explosive Forces

"A psychiatrist," said Mr. Justice Barry, "had explosive forces under his control, and if they were released the consequences might be disastrous. He must exercise the very greatest care in dealing with the dark secrets of the human mind." Dr. Werner had agreed that he departed from standard practice in originating and continuing the long course of social contacts with Miss Landau, but said that this was justified in the exceptional circumstances of the case. However, one witness (Dr. David Stafford Clark) had said that social contact with the patient gave rise to difficulties, and if they were unavoidable the doctor should withdraw from the case. In the opinion of the court there was not a body of opinion which would have thought it desirable to take out a woman in a highly emotional state and already in love with the doctor. In the circumstances, Dr. Werner had been negligent, although with the best intentions in the world.

LADY HOARE AND THE LONDON CLINIC

[FROM OUR LEGAL CORRESPONDENT]

On March 7 the Court of Appeal rejected Lady Hoare's appeal against the order staying the fresh proceedings taken out by her against the London Clinic in the Bloomsbury County Court (*Journal*, October 22, 1960, p. 1246) following her unsuccessful proceedings in the House of Lords. Leave to appeal to the House of Lords was refused (*The Times*, March 8).

Vital Statistics

Influenza

In the week ending March 4 there were 340 (568) deaths from influenza in England and Wales, 657 (938) from pneumonia, and 858 (981) from bronchitis (deaths in the previous week in parentheses). New claims to sickness benefit decreased to only slightly over the level of a year ago, and influenza appeared to be declining in all parts of England and Wales.

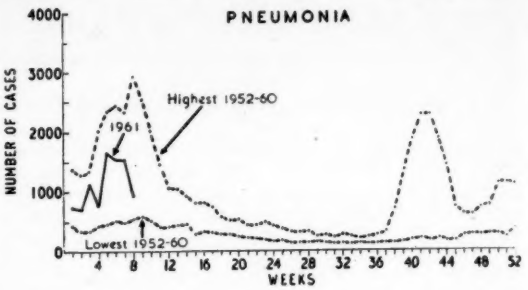
Road Accidents in 1960

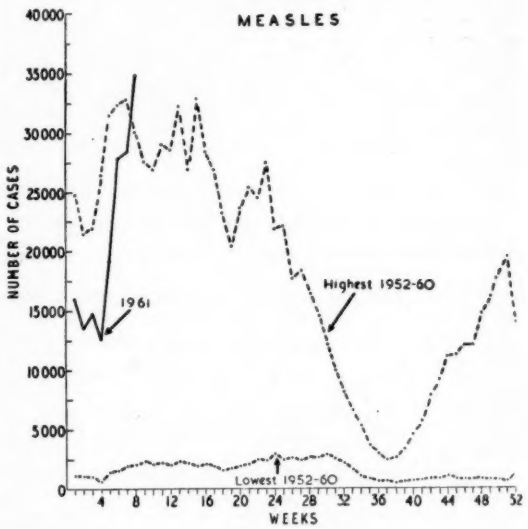
During December, 1960, there were 764 deaths from road accidents (117 fewer than in the previous year), and this brought the death roll for the year up to 6,970, with 84,443 seriously injured. The fatal casualties were 450 (7%) more than in 1959. The increase in motor traffic was estimated to be 7%. The outstanding features of the year's figures were a 19% increase in the number of deaths and a 15% increase in total casualties among drivers of cars and taxis (mainly private cars). Deaths of pedestrians increased by 7%, but fewer motor-cyclists and pedal cyclists were killed in 1961 than in 1960. But with the increased use of mopeds and scooters, riders and passengers on both types of machine suffered increases in deaths and injuries: 278 motor-scooter riders and passengers were killed, a rise of 32%.

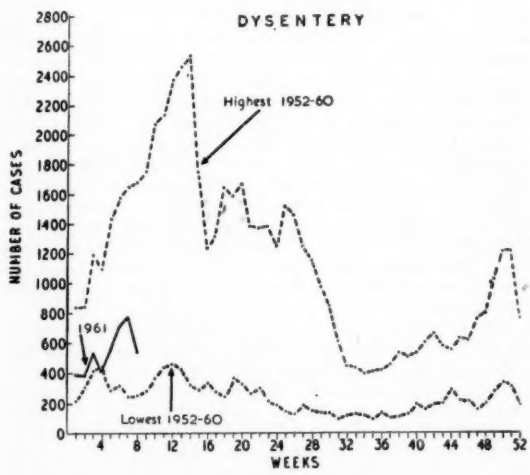
In France during 1960 road accidents caused the deaths of 5,804 persons, and 96,889 were injured.

Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the years 1952–60 are shown thus ------, the figures for 1961 thus———. Except for the curves showing notifications in 1961, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.







Industrial Accidents and Diseases

The number of workpeople (other than seamen) in the United Kingdom whose deaths from accidents in the course of their employment were reported in January was 88, compared with 115 in the previous month and 72 in January, 1960.

The number of cases of industrial disease in the United Kingdom reported during January were as follows: lead poisoning 4, aniline poisoning 1, anthrax 2, epitheliomatous ulceration 7, chrome ulceration 16, total 30. There were no deaths.

Infectious Diseases

Areas where the numbers of notifications were high in the latest two weeks for which figures are available.

Measles	Week Ending Feb. 25	Mar. 4
Durham	1,369	1,669
Sunderland C.B.	395	516
Essex	2,336	2,419
West Ham C.B.	154	260
Harlow U.D.	381	181
Romford M.B.	235	207
Hampshire	1,339	1,642
Southampton C.B.	328	558
Herefordshire	140	322
Hereford M.B.	103	246
Kent	1,630	1,735
Chislehurst and Sidcup U.D.	149	207
Lancashire	2,386	2,369
Bolton C.B.	199	220
Liverpool C.B.	152	199
Manchester C.B.	323	313
London	3,339	3,403
Camberwell	229	245
Islington	230	179
Lambeth	211	279
Lewisham	348	372
Wandsworth	342	402
Woolwich	220	203
Middlesex	2,032	2,373
Enfield M.B.	127	215
Harrow M.B.	165	197
Hayes and Harlington U.D.	117	215
Willesden M.B.	271	276
Northumberland	640	583
Newcastle upon Tyne C.B.	247	260
Wolverhampton C.B.	146	126
Warwickshire	2,497	2,802
Birmingham C.B.	1,235	1,318
Coventry C.B.	556	701
Solihull M.B.	157	258
Wiltshire	288	345
Swindon M.B.	214	221
Yorkshire East Riding	809	813
Kingston upon Hull C.B.	576	573
Yorkshire West Riding	2,504	2,147
Leeds C.B.	220	254
Sheffield C.B.	405	333
Glamorganshire	1,117	1,047
Cardiff C.B.	325	376
Dysentery		
Devonshire	17	19
Exeter C.B.	13	16
Essex	28	69
Chigwell U.D.	6	25
Wanstead and Woodford M.B.	2	16
Herefordshire	10	28
Hereford R.D.	3	19
Middlesex	12	26
Hendon M.B.	0	15
Worcestershire	3	16
Bromsgrove U.D.	0	12
Yorkshire West Riding	144	226
Bradford C.B.	17	17
Huddersfield C.B.	1	30
Leeds C.B.	35	72
Thorne R.D.	16	21
Diphtheria		
Staffordshire	0	4
Willenhall U.D.	0	4
Warwickshire	1	3
Birmingham C.B.	1	3

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **February 25** (No. 8) and corresponding week 1960.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the whole of England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES	1961 Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	1960 Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	6	4	2	1		3	0	0	1	2
Dysentery	539	28	90	8	3	1,667	177	238	32	3
Encephalitis, acute	2	0		0		3	0	2	0	
Enteric fever:										
Typhoid	2	1	0	0		0	0	0	0	3
Paratyphoid	1	0	1(B)	0		4	0	0	0	
Food-poisoning	101	14	10	2		146	29	7	0	
Infective enteritis or diarrhoea under 2 years				7	22				13	16
Measles*	34,863	3339	678	459	516	2,131	60	54	3	56
Meningococcal infection	39	5	5	1	3	20	2			
Ophthalmia neonatorum	15	1	4	0		16	1	5	0	
Pneumonia†	938	58	411	10	23	550	10	237	7	5
Poliomyelitis, acute:										
Paralytic	1	1	0	0		1	0	0	0	4
Non-paralytic	1	0	1			3	1	2		
Puerperal fever§	175	16	15	0		192	35	10	2	1
Scarlet fever	480	46	39	23	8	1,126	44	73	39	14
Tuberculosis:										
Respiratory	414	50	65	17		432	62	66	13	
Non-respiratory	78	4	12	3		57	1	8	2	
Whooping-cough	753	46	93	10	83	856	82	174	5	31

DEATHS	1961 Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	1960 Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	0	0	0	0	0	0	0	0	0	0
Dysentery	0	0		0		0	0		0	
Encephalitis, acute		0			0		1			0
Enteric fever	0	0	0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years	13	2	0	0	1		0	1	0	2
Influenza	568	21	30	10	17	56	5	0	0	0
Measles		1	0	0	1		0	0	0	0
Meningococcal infection		1	1				0	1		
Pneumonia	1,232	77	65	40	13	820	52	44	27	7
Poliomyelitis, acute	0	0		0	0	0	0		0	0
Scarlet fever		0	0	0	0		0	0	0	0
Tuberculosis:										
Respiratory	90	8	7	3	1	88	11	9	0	8
Non-respiratory		1		0	0		2	0	0	0
Whooping-cough	1	0	0	0	1	1	0	0	0	0
Deaths 0–1 year	334	29	27	9	7	368	29	41	10	10
Deaths (excluding stillbirths)	13,030	942	746	178	203	12,520	967	794	184	186
LIVE BIRTHS	15,711	1312	1041	283	374	15,461	1315	1049	290	373
STILLBIRTHS	305	20	30			346	32	28		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Medical News

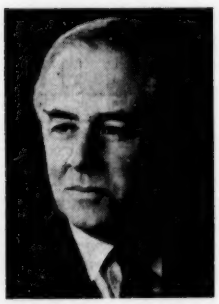
National Clinical Research Centre

Plans were announced in the House of Commons on March 13 for linking the new district hospital which is planned for Northwick Park, Middlesex, with the national clinical research centre to be established on the same site by the Medical Research Council. (See *B.M.J.* annotation, July 23, 1960, p. 286.) Professor J. R. SQUIRE is director-designate of the centre, which will be close enough to the National Institute for Medical Research at Mill Hill for effective collaboration and use of its resources. The hospital will provide some 500 beds for the needs of the local community, and up to 200 additional beds, grouped in clinical units, for the special investigation of patients and for specialized forms of treatment.

Chair of Psychiatry, St. George's Hospital Medical School

Dr. DESMOND CURRAN, senior psychiatrist at St. George's Hospital and civil consultant in psychological medicine to the Royal Navy, has been appointed to the newly created London University chair of psychiatry tenable at St. George's Hospital Medical School as from October 1.

Dr. Curran, who was born in 1903, was educated at Wellington, Trinity College, Cambridge, and St. George's Hospital. He graduated M.B., B.Chir. in 1928, took his D.P.M. in 1930, and was elected F.R.C.P. in 1937. He was awarded the Royal Medico-Psychological Society's Gaskell gold medal in 1933. He worked successively at St. George's, Bethlem Royal Hospital, and the Maida Vale Hospital for Nervous Diseases before being appointed A.M.O. at the Maudsley Hospital in 1930. He worked there in various capacities until 1937, interrupted by a year spent in the United States as a Rockefeller Travelling Fellow—mainly at the Phipps Psychiatric Clinic and the Johns Hopkins Hospital, Baltimore. During the war he was consultant in psychological medicine to the Royal Navy and helped to organize its neuropsychiatric service. He has served the Royal College of Physicians, the Royal Society of Medicine, the R.M.P.A., and the B.M.A. in many ways, and has done much committee work for them and for various Government and departmental committees, among them being the Wolfenden Committee on Homosexual Offences and Prostitution. He is a member of the Clinical Psychiatry Committee of the Medical Research Council. Dr. Curran's publications include *Psychological Medicine* (with Dr. M. PARTRIDGE: 5th edition, 1961), and sections, chapters, and articles in many other books and journals. His particular interests have included toxic confusional states, administrative and social problems—some closely associated with forensic psychiatry and psychopathic personalities—prefrontal leucotomy, and psychiatric education in medicine.



Medical Committee Against Racial Discrimination in South Africa

The Medical Committee Against Racial Discrimination in South Africa, which was formed last year (see *B.M.J.*, 1960, May 28, p. 1651 ; July 2, p. 81), has issued a summary of its activities. The committee made vigorous protests about the imprisonment of South African medical practitioners detained under the Emergency Regulations: the doctors were released last September. Research is being done on the effects that apartheid policies are having on the teaching and practice of medicine and nursing. The committee has received many protests about the medical schools of Witwatersrand (Johannesburg) and Capetown being forced to join those of Pretoria and Stellenbosch in refusing to accept non-white medical students. The South African Government intends the Durban Medical School itself to come under the Separate Universities Act. The committee aims to co-ordinate local and overseas protests in support of the Durban Faculty, and hopes to help place for medical or dental training any eligible students who can leave South Africa. For these and other projects financial support is needed. The secretary is Dr. ELEANOR ETTLINGER, 20 Lansdowne Crescent, London W.11.

Moorfields Research Scholarship

The Moorfields Research Scholarship for 1962 (value approximately £300 sterling) will be awarded for the best essay in English on "The Clinical Value of Tonometry and Tonography." The prize is open to all nationalities, and the essay should be sent to the Director of Research, Institute of Ophthalmology, Judd Street, London W.C.1, by July 31, 1962. It should be signed by a motto or a pseudonym, and accompanied by a sealed envelope containing the name of the author, the motto to be shown on the outside.

"British Medical Students' Journal"

On the cover of the spring issue of the *B.M.S.J.* a worried student prays fervently before a goddess labelled "Literature," who is a cut-out made of scribbled notes such as "? sibs ? heart." Inside the issue are articles on an international students' meeting in Scandinavia, the unit for students with tuberculosis at Pinewood Hospital, Berkshire, the Inter-Hospitals Brighton stroll—with an alarming portrait of feet that have taken part—climbing in Wales, and an apartheid hospital near Johannesburg. (Price 6d. to members, 1s. to non-members, from B.M.S.A., B.M.A. House, Tavistock Square, London W.C.1.)

Medical Society of London

The 121st anniversary dinner of the Medical Society of London was held at the Park Lane Hotel on March 9, with Mr. NILS L. ECKHOFF, the president of the Society, in the chair. Mr. Justice SALMON proposed the main toast of the evening, and in his reply Mr. Eckhoff spoke briefly of the Society's activities during the year. Dr. JOSEPH SMART proposed the health of the visitors, and Mr. A. C. H. BELL, President of the Royal College of Obstetricians and Gynaecologists, replied.

New U.S. Surgeon-general

Dr. LUTHER L. TERRY was recently appointed surgeon-general of the United States by President KENNEDY in succession to Dr. LEROY BURNEY. The surgeon-general directs the activities of the U.S. Public Health Service, which include the National Institutes of Health.

Dr. Terry, who was born in 1911, graduated from Tulane University School of Medicine in 1935. After serving in hospitals in Cleveland, he taught medicine, preventive medicine, and public health at Washington University, St. Louis, Mo., and the University of Texas. He was assistant professor in these disciplines at Texas from 1941 to 1942. In 1942 he entered the Public Health Service. After instructing in medicine (part-time) at Johns Hopkins University School of Medicine for some years he became assistant professor in medicine there fr[om] 1953 to the present day. In 1950 to 1958 he was chief of t[he] general medicine and experimental therapeutics branch o[f] the National Heart Institute, and in 1958 was appointed ass[ociate] director. He has undertaken research on enzyme-inhibiting d[rugs] in the treatment of hypertension. (Photograph by co[urtesy] of U.S. Public Health Service.)

W.H.O. Budget for 1962

The World Health Assembly has adopted a working budget of $23,607,180 for the World Health Organization in 1962. This represents an increase of 19.3% over the working budget for 1961, and includes $2m. toward financing the malaria eradication programme. Hitherto, this has been financed from voluntary contributions. These

have proved to be inadequate: the United States has provided more than 90% of the contributions that have been received.

"Therapeutikon"

The first number of a new Italian journal, *Therapeutikon*, was published in December last year. It is a bi-monthly review of general medicine with particular emphasis on clinical and experimental pharmacology. It is hoped to provide summaries in English and French for the articles printed. The editor is Dr. A. M. MICHELAZZI, and inquiries should be addressed to Direzione della Revista, *Therapeutikon*, Casella Postale N.559, Pisa, Italy. The subscription rate is L.4,500 a year.

"Kybernetik"

Kybernetik is a new German journal dealing with the transmission and processing of information, and with control processes both in organisms and automata. It will include experimental and theoretical findings on sensory processes and micro- and macrophysiology of the central nervous system in relation to information handling. To ensure rapid publication individually priced issues will appear as the papers become available, but the subscription for 1961 will not exceed DM.80. Inquiries should be addressed to the publishers, Springer-Verlag, 3 Heidelberger Platz, Berlin-Wilmersdorf.

Memorial Center Fellowship

The Memorial Center for Cancer and Allied Diseases is offering a one-year Fellowship in Medical Neoplasia from July 1, 1962. Details may be obtained from Dr. H. D. DIAMOND at the Center, 444 East 68th Street, New York 21, N.Y., U.S.A.

R.I.B.A. Alfred Bossom Research Fellowship for Postgraduate Research

The Royal Institute of British Architects has awarded the Alfred Bossom Research Fellowship for 1961 jointly to Mr. P. COWAN and Mr. R. Moss. They will investigate problems associated with the reconstruction of urban hospitals and would appreciate information from anyone who has had experience in this field. Correspondence should be addressed to the two research fellows, c/o R.I.B.A., 66 Portland Place, London W.1.

New Infirmary, Royal Hospital, Chelsea

A new infirmary for the 400 Chelsea Pensioners at the Royal Hospital, Chelsea, was opened by QUEEN ELIZABETH THE QUEEN MOTHER last month. It replaces the old infirmary built by Sir John Soane in 1810 which was destroyed by bombing in 1941.

The infirmary, which cost £200,000, caters for the needs of the acute and chronic sick among the In-pensioners, with the exception of major surgery and other specialized procedures. Its wards have six beds each and there are eight single rooms for very ill patients. There is an out-patient department, a physiotherapy department, and a radiographic department. The day-room curtains are patterned with soldiers wearing historical regimental uniforms, and with other regimental details. The beds in the wards are covered with the traditional scarlet blankets believed to have been introduced by Florence Nightingale.

(*Crown Copyright*

New infirmary (designed by the Ministry of Works), Royal Hospital, Chelsea.

People in the News

Sir ARTHUR PORRITT, P.R.C.S., was made an Honorary Fellow of the Royal Australasian College of Surgeons on February 20 at Melbourne.

COMING EVENTS

Anglo-American Medical Society.—First annual general meeting, March 22, 8.30 p.m., Cambridge University Department of Biochemistry, Tennis Court Road, Cambridge. Sherry 8 p.m.

Association of Industrial Medical Officers.—92nd meeting, March 24, 10 a.m., London School of Hygiene and Tropical Medicine, Keppel Street, London W.C.1; March 25, 10 a.m., Maudsley Hospital, Denmark Hill, London S.E.5. Details from Honorary Secretary, 47 Lincoln's Inn Fields, London W.C.2.

B.M.S.A. National Clinical Conference.—Cardiff, April 4–7. Subjects: "Mental Health," "Pneumoconiosis." Details from B.M.S.A., B.M.A. House, Tavistock Square, London W.C.1.

Institute of Urology.—Week-end course, "Medical Aspects of Renal Diseases," April 7–9. See advertisement p. 61.

National Association for Mental Health and Department of Psychological Medicine, King's College, Durham University.—Course for assistant medical officers working in Maternity and Child Welfare and/or School Health Services. "Problems of Growth and Development in Childhood," April 10–14, Henderson Hall of Residence, Cochrane Park, Newcastle upon Tyne 7. Details from, and applications to, N.A.M.H., 9 Mount Preston, Leeds 2. (Tel. 23926.)

Family Planning Association.—Training service for medical practitioners. Details on advertisement p. 61.

Institute for Study and Treatment of Delinquency.—Study tour of Denmark, May 21–31. Visits to State prison, institute for criminal psychopaths, women's open prison, alcoholics' clinic, probation hostel, and penal workhouse for old recidivists. Details from General Secretary, I.S.T.D., 8 Bourdon Street, London W.1. (MAYfair 3472.)

Mental After-Care Association.—81st Annual Meeting March 23, 3 p.m., Worshipful Company of Haberdashers' Hall, Staining Lane, London E.C.2. Speakers: Very Rev. RABBI ISRAEL BRODIE (Chief Rabbi) and Dr. J. C. SAWLE THOMAS.

NEW ISSUES OF SPECIALIST JOURNALS

The journals listed below are obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

JOURNAL OF NEUROLOGY, NEUROSURGERY, AND PSYCHIATRY

Craniopharyngioma in the Elderly. R. W. Ross Russell and J. B. Pennybacker.
The Effect of Ageing upon Physiological Tremor. John Marshall.
Quadriceps Myopathy Occurring in Middle Age. J. W. Aldren Turner and K. W. G. Heathfield.
Origin of Echoes in the Echoencephalogram. Brita Lithander.
Cerebral Trauma in Infancy and Intellectual Defect. R. C. Oldfield and Moyra Williams.
Observations on Selective Leucotomy. Walpole Lewin.
The Size and Growth of the Human Optic Nerve. Peter E. Sylvester and Kevser Ari.
The Electroencephalogram in Congenital Hypothyroidism: A Study of 10 Cases. Eric A. Nieman.
The Electroencephalographic Diagnosis of Manifest and Latent "Delirium" with Particular Reference to that Complicating Hepatic Cirrhosis. John Laidlaw and A. E. Read.
The Rigid Form of Huntington's Disease. A. M. G. Campbell, Beryl Corner, R. M. Norman, and H. Urich.
Response of Normal and Multiple Sclerotic Subjects to Typhoid-Paratyphoid Vaccine Injections. E. J. Field, C. A. Green, and Henry Miller.
A Huge Osteoma in the Anterior Cranial Fossa. Vl. Hudolin, D. Riessner, S. Kadrnka, and M. Knežević.
An Internal Carotid Aneurysm in the Petrous Temporal Bone. Sami Guirguis and Fathy W. Tadros.
Chronic Arachnoidal Cysts of the Middle Cranial Fossa and Their Relation to Trauma. P. Tiberin and J. Gruszkiewicz.
Proceedings of the Society of British Neurological Surgeons: 62nd Meeting. Book Reviews.

Volume 24, No. 1. (Quarterly; £3 annually.)

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Monday, March 20

HUNTERIAN SOCIETY.—At Talbot Restaurant, 64 London Wall, E.C., 7 for 7.30 p.m., dinner meeting. 8.30 p.m., discussion: Educational Problems in Children. To be opened by Sir Wilfrid Sheldon and Professor D. V. Hubble.

LONDON UNIVERSITY.—At King's College, 5.30 p.m., Halliburton Lecture in Physiology by Dr. S. J. Sarnoff (Bethesda, U.S.A.): Homoeometric Autoregulation in the Heart.

POSTGRADUATE MEDICAL SCHOOL OF LONDON.—4 p.m., Dr. R. I. S. Bayliss: Treatment of Oedema.

Tuesday, March 21

CHARING CROSS HOSPITAL MEDICAL SCHOOL.—6 p.m., Professor Hans H. Ussing (Copenhagen): Physiological Significance of Active Sodium Transport.

FOUNTAIN HOSPITAL.—5.30 p.m., Dr. J. Tizard: Small Unit for the Care of Severely Subnormal Children. Film: Mentally Handicapped Children Growing Up—The Brooklands Experiment.

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. J. A. Dudgeon: Virus Infections (II).

LONDON UNIVERSITY.—(1) At London School of Hygiene and Tropical Medicine, 5.30 p.m., special university lecture by Professor H. R. Mühlemann (Zurich): Trends in Experimental Caries Research. (2) At King's College, 5.30 p.m., Halliburton Lecture in Physiology by Dr. S. J. Sarnoff (Bethesda, U.S.A.): Activity Graded Sympatholysis in the Vascular Bed Supplying Muscles.

MANCHESTER MEDICAL SOCIETY.—At Large Anatomy Theatre, Medical School, Manchester University, 4 for 4.30 p.m., University Lecture on the History of Medicine by Sir John Charles: Theodore de Mayerne, Archiater.

WEST END HOSPITAL FOR NEUROLOGY AND NEUROSURGERY.—5.30 p.m., Mr. M. A. Bennett: Stereotaxis.

Wednesday, March 22

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. R. W. Riddell: Anti-fungal Agents.

INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. Lynne McA. Reid: Pathological Basis of Unilateral Transradiancy of the Lung.

MANCHESTER MEDICAL SOCIETY: SECTION OF MEDICINE.—At Large Anatomy Theatre, Medical School, Manchester University, 4 for 4.30 p.m., Presidential Address by Dr. E. D. Gray: Some Developments in Diagnostic Radiology.

POSTGRADUATE MEDICAL SCHOOL OF LONDON.—2 p.m., Professor T. Symington: Nature of the Actiology and Pathogenesis of Adrenocortical Lesions.

ROYAL COLLEGE OF SURGEONS OF ENGLAND AND INSTITUTE OF UROLOGY.—At Royal College of Surgeons of England, 5 p.m., Urology Lecture by Mr. Ashton Miller: Prevention of Infection in Urology.

ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE.—3.30 p.m., Dr. M. E. M. Herford: Health of Young People in Industry (illustrated).

ROYAL SOCIETY OF HEALTH.—At Alexandra Hall, Halifax, 10 a.m., Professor C. E. Lumsden: Some Aspects of Multiple Sclerosis; Dr. R. C. Laverick: Noise Nuisance; Mr. A. W. Perry: Treatment of Industry in Smoke Control Areas

SOCIETY OF MEDICAL OFFICERS OF HEALTH: HOME COUNTIES BRANCH.—At Room 142, London School of Hygiene and Tropical Medicine, 2.45 p.m., Professor H. J. Eysenck: Causes and Cures of Neuroses.

Thursday, March 23

BELMONT HOSPITAL CLINICAL SOCIETY.—8 p.m., Dr. John Cowie: The Approved School Girl.

INSTITUTE OF NEUROLOGY.—5.30 p.m., Professor V. B. Mountcastle (Baltimore, U.S.A.): Functional Meaning of Duality in the Somatic Afferent System.

INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.—At Chelsea Hospital for Women 4.30 p.m., Professor Lee Buxton (Yale): Post-coital Test and Treatment of Male Infertility.

LIVERPOOL MEDICAL INSTITUTION.—Annual Meeting.

LONDON JEWISH HOSPITAL MEDICAL SOCIETY.—At Selbys, 6 Hanover Street, W., 6.45 p.m., annual dinner-dance.

ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Hunterian Lecture by Professor W. B. Jennett: Epilepsy After Blunt Head Injury.

SOCIETY OF MEDICAL OFFICERS OF HEALTH: SOUTHERN BRANCH.—At Bournemouth Town Hall, 3 p.m., Mr. H. J. Wright: I.Q. 100 and All That.

Friday, March 24

INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Mr. M. Paneth: clinical demonstration.

INSTITUTE OF LARYNGOLOGY AND OTOLOGY.—5.30 p.m., Mr. E. J. Radley-Smith: Brain Abscess.

SOCIETY OF MEDICAL OFFICERS OF HEALTH: WELSH BRANCH.—At B.M.A. House, 195 Newport Road, Cardiff, 6.30 p.m., Dr. A. R. Culley: Hospitals in America.

Saturday, March 25

INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.—At Hammersmith Hospital, 11.15 a.m., Professor Lee Buxton (Yale): Treatment of the Abnormal Fallopian Tube in Infertility.

APPOINTMENTS

BEARD, A. W., M.B., B.Chir., M.R.C.P., D.P.M., Consultant Physician in Psychological Medicine, Middlesex Hospital, London W.

BIRMINGHAM REGIONAL HOSPITAL BOARD.—W. H. Davies, M.Chir., F.R.C.S., Part-time Consultant Surgeon to Herefordshire Group; G. Clarke, M.B., Ch.B., F.F.A. R.C.S., D.A., Part-time Consultant Anaesthetist to Stoke-on-Trent Group; G. W. Goulden, M.R.C.S., L.R.C.P., Whole-time Assistant Psychiatrist (S.H.M.O.), Monyhull Hospital; J. McQuillan, M.B., B.Ch., D.P.M., Whole-time Consultant Psychiatrist and Medical Superintendent, Burghill and Holme Lacy Hospitals; R. A. Browne, M.B., B.Ch., D.P.M., Whole-time Consultant Psychiatrist and Medical Superintendent, Coleshill Hall Hospital; W. J. R. Anderson, M.B., Ch.B., M.R.C.O.G., Part-time Consultant Obstetrician and Gynaecologist to Coventry and South Warwickshire Groups; G. C. Slee, M.Ch.Orth., F.R.C.S., Part-time Consultant Orthopaedic Surgeon to Hereford Group and Robert Jones and Agnes Hunt Orthopaedic Hospital; G. K. Laxton, M.B., Ch.B., M.R.C.P.Ed., D.T.M.&H., Whole-time Consultant Physician (Geriatrics) to Coventry Group; J. W. Price, M.B., Ch.B., L.D.S., Whole-time Senior Hospital Dental Officer to Mid-Staffordshire Mental and Stoke-on-Trent Groups; A. B. McL. Currie, M.B., Ch.B., F.R.C.S.Ed., Whole-time Consultant Surgeon to Birmingham (Selly Oak) Group.

EAST ANGLIAN REGIONAL HOSPITAL BOARD.—Jack D. Pryce, M.D., Consultant Pathologist, Ipswich and East Suffolk Area; C. G. A. Thomas, B.M., B.Ch., M.R.C.P., Consultant Bacteriologist, Norfolk and Norwich Area; Elizabeth L. Brown, M.B., Ch.B., M.R.C.P.Ed., Assistant Chest Physician, Norwich and East Norfolk Chest Clinic and Mass Radiography Service; M. Gunasheela, M.B., Surgical Registrar, West Suffolk General Hospital; J. J. Breen, M.B., B.S., Surgical Registrar, United Norwich Hospitals; G. C. Jhaveri, M.B., B.S., Registrar in Radiology, Norfolk and Norwich Hospital.

HOSPITAL FOR SICK CHILDREN, Great Ormond Street, London W.C.—P. Field, M.B., B.S., F.R.C.S., Registrar in Thoracic Surgery; Joyce M. Stephen, M.B., B.S., D.P.M., Part-time Medical Officer in the Department of Psychological Medicine; Phillida M. Frost, M.B., B.S., F.F.A. R.C.S., D.A., Resident Anaesthetic Registrar; F. G. Fennell, L.R.C.P.&S.I., D.L.O., Senior Registrar to Ear, Nose, and Throat Department; Sonia R. Dias Bandaranaike, M.B., B.Chir., and A. R. R. Cain, B.M., B.Ch., D.Obst.R.C.O.G., House Physicians; J. D. Jefferies, M.B., Ch.B., House Surgeon.

MANCHESTER REGIONAL HOSPITAL BOARD.—C. D. R. Pengelly, M.D., M.R.C.P., M.R.C.P.Ed., Consultant Physician (seven half-days weekly), North and Mid-Cheshire Group of Hospitals; H. W. Wilson, M.B., Ch.B., M.R.C.O.G., Consultant Obstetrician and Gynaecologist (eight half-days weekly), Bury and Rossendale Group of Hospitals; B. B. Beeson, M.B., Ch.B., M.R.C.P.Ed., D.Path., Whole-time Consultant Pathologist, Lancaster and Kendal and Lancaster Moor Groups of Hospitals; M. M. Patricia Leahy, L.R.C.P.&S.I., D.A., Whole-time Assistant Anaesthetist, Bury and Rossendale Group of Hospitals; L. Walker, M.R.C.S., L.R.C.P., D.A., Assistant Anaesthetist (nine half-days weekly), North and Mid-Cheshire Group of Hospitals; F. Kelly, M.B., B.Ch., L.M., D.P.H., D.M.R.T., Whole-time Assistant Radiotherapist, Christie Hospital and Holt Radium Institute; P. Roughead, M.B., Ch.B., D.P.H., D.P.M., Whole-time Consultant Psychiatrist, Springfield Hospital, Manchester; J. Sharp, M.D., M.R.C.P., Consultant Physician (nine half-days weekly), Stockport and Buxton and South Manchester Groups of Hospitals; J. Wilks, M.B., F.R.C.S., Consultant General Surgeon (nine half-days weekly), Bolton and District Group of Hospitals; D. Hay, M.B., B.Ch., B.A.O., M.R.C.O.G., Consultant Obstetrician and Gynaecologist (eight half-days weekly), North Manchester Group of Hospitals; L. Poller, M.D., Whole-time Consultant Pathologist, South Manchester Group of Hospitals; R. H. L. Brown, M.B., Ch.B., Whole-time Senior Casualty Officer, Ashton-under-Lyne General Hospital; B. N. Baijal, M.B., F.R.C.S., Whole-time Senior Casualty Officer, Westmorland County Hospital, Kendal; M. H. Hall, M.R.C.S., L.R.C.P., Whole-time Senior Casualty Officer, Preston Royal Infirmary.

MOLONY, J., M.D., Consultant in Physical Medicine, St. Vincent's Hospital, Dublin.

MULDOWNEY, F. P., M.D., M.R.C.P.Ed., Assistant in the Department of Medicine, University College, Dublin, and Assistant Visiting Physician, St. Vincent's Hospital, Dublin.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Reed.—On January 15, 1961, to Elisabeth, wife of Dr. Ernest Spencer Reed, of Denpasar, Bali, Indonesia, a daughter—Nichola.

DEATHS

Armitage.—On February 17, 1961, in a Bath nursing-home, Charles Ernest Augustus Armitage, M.B., B.C., aged 83.

Cowin.—On February 23, 1961, at Elmdene, Chiddingfold, Surrey, Douglas Henry Fawcett Cowin, M.R.C.S., L.R.C.P., Lieutenant-Colonel, I.M.S., retired, aged 87.

Creasy.—On February 21, 1961, at Priors, Abbots Kerswell, Devon, Rolf Creasy, M.B., B.S.

Day.—On February 21, 1961, at Shrublands Nursing Home, Croydon, Dorothy Lili Crundall Day, M.R.C.S., L.R.C.P., of Amberley, 59 Addiscombe Road, Croydon, Surrey.

Derry.—On February 20, 1961, at Radwinter, near Saffron Walden, Douglas Erith Derry, *M.C.*, F.R.C.S., late of Cairo, aged 86.

Dibb.—On February 4, 1961, at Bramley Park, Rotherham, Yorks, William Land Dibb, M.B., Ch.B., D.P.H., aged 76.

Dobbin.—On February 14, 1961, John Robson Dobbin, M.B., Ch.B., of Staffords, Ottery St. Mary, Devon, aged 80.

Earl.—On February 16, 1961, at Wynstead, Manor Road, St. Marychurch, Torquay, Ernest Hugh Cecil Earl, M.R.C.P.I., aged 54.

Everdell.—On February 20, 1961, Edna Traill Everdell, M.B., B.S., D.P.H., of 220 Western Way, Ponteland, Newcastle upon Tyne.

Macarthur.—On February 17, 1961, in hospital, John Macarthur, M.R.C.S., L.R.C.P., D.P.M., of 46 Park Way, Maidstone, Kent, aged 78.

Mann.—On February 18, 1961, at Guy's Hospital, London S.E., Harold Charles Corry Mann, O.B.E., M.D., of Junior Carlton Club, London S.W.

Mason.—On February 13, 1961, Charles Arthur Mason, M.B., Ch.B., D.P.H., formerly of Cockermouth, Cumberland.

Maxwell.—On February 21, 1961, George Henry Hope Maxwell, M.B., Ch.B., D.P.H., Group Captain, R.A.F., retired.

Milner.—On February 13, 1961, at Burton Wirral, William Arnold Milner, M.R.C.S., L.R.C.P., aged 80.

Mitchell.—On February 14, 1961, Herbert Mitchell, M.D., Major R.A.M.C., of Barracks Stud, Nash, near Bletchley.

Mitra.—On January 9, 1961, at Little Aden, Aden Colony, Asok Kumar Mitra, M.B., D.T.M.&H., D.P.H., aged 42.

Nicholson.—On February 22, 1961, at St. Mary's Private Hospital, Bristol, Cuthbert John Nicholson, M.R.C.S., L.R.C.P., aged 76.

Price.—On February 16, 1961, at 4 Dunraven Road, Swansea, Frederick Noel Ritchie Price, M.B., Ch.B.

Ross.—On February 21, 1961, in Cardiff, Henry Alexander Ross, M.B., Ch.B., D.P.H., aged 63.

Sharp.—On February 21, 1961, at 60 Leeds Road, Harrogate, Alfred Cecil Sharp, M.D.

Sinclair.—On February 21, 1961, James Denny Sinclair, M.B., Ch.B., of 381 High Road, Streatham, London S.W.

Smith.—On February 22, 1961, in Hong Kong, Hugh Smith, M.B.E., M.D., D.M.R.D., late of Bearsden, Glasgow, aged 58.

Van Someren.—On February 8, 1961, at 5 Craigleith Hill Gardens, Edinburgh, Richard Kenneth Alexander Van Someren, F.R.C.S.Ed.

Veale.—On March 8, 1961, Frederick John de Coverly Veale, M.D., of 60 Kewstoke Road, Stoke Bishop, Bristol, aged 90.

Any Questions ?

We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.

Sensitivity to Nickel

Q.—*A patient has become highly skin-sensitive to nickel, as shown by patch test. Is nickel a constituent of any domestic ware which she should stop using or a component of any article of diet?*

A.—It is presumed that the question does not refer to an industrial dermatitis but to that occurring commonly in women from a contact dermatitis from allergy to nickel, usually beginning under the metal parts of suspenders. Brassiere clips, wrist watches, and various pieces of jewellery containing nickel can all cause a primary dermatitis at the contact sites. The secondary eczematous eruption on the arm flexures, eyelids, sides of neck, and inner thigh may become of much greater importance than the primary lesion. The mechanism of the secondary eczematous dermatitis is unknown, but does not seem to be related to direct contact with nickel.[1] Nickel in the diet, even if present, would seem to be unlikely as a cause of dermatitis, since it is the exceptional affinity of keratin for nickel which is responsible for dermatitis arising. Keratin will take up the nickel ions which are released in sweat. Even one part per million of nickel will be taken up by keratin.

In the very acute stage of nickel dermatitis, it would perhaps be unwise to handle nickel objects—and there may be many in a woman's handbag. Yet, so long as nickel is not actually worn, it seems quite safe[2] to handle most metallic objects even if they contain nickel.

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1 Calnan, C. D., and Wells, G. C., *Brit. med. J.*, 1956, **1**, 1265.
2 Loewenthal, L. J. A. *The Eczemas*, 1954. Livingstone, Edinburgh and London.

Intra-arterial Transfusion

Q.—*What is the current opinion on the use of intra-arterial blood transfusion in a case of severe haemorrhage? Can stored, citrated blood be used?*

A.—The case for intra-arterial transfusion was carefully examined by Case *et al.* In dogs who were bled to hypotensive levels the coronary flow and arterial pressure responded as rapidly and to the same extent whether the blood was transfused intravenously or intra-arterially. They concluded that the only theoretical advantage of intra-arterial infusion was when, owing to cardiac arrest or almost completely ineffective contraction, the blood could not be passed from the venous side to the arterial side. They considered that this possible advantage would be offset by the extra delay in setting up intra-arterial infusion and the risk of gangrene to the extremities.

If his view is accepted it becomes a little academic to discuss the composition of the blood which would be used if arterial transfusion was attempted. Nevertheless, if an answer were required it would be that, since, when blood is transfused into the aorta there is a chance that some of it will reach the coronary vessels after very little mixture with the recipient's own blood, ideally only fresh heparinized blood should be used. The problem is, of course, similar to that which arises when massive amounts of blood have to be infused into the patient during operations on the heart. For this purpose it has been found convenient to use E.D.T.A. as an anticoagulant rather than citrate, because the amount of calcium required to neutralize E.D.T.A. can be more exactly calculated than the amount required to neutralize citrate. The method is to take the blood into a solution containing E.D.T.A. and store it for two or three days if necessary; immediately before operation heparin is added, followed by the amount of calcium calculated to combine with all the E.D.T.A. present.[2] This procedure overcomes the potential risks of citrate, but it still does not deal with all the disadvantages of using stored blood. Nevertheless, it is probably the best available compromise, since it is very difficult to supply fresh heparinized blood in large quantities, particularly under emergency conditions.

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2 Smith, W. W., Brown, I. W., jun., Young, W. G., jun., and Sealy, W. C., *J. thorac. Surg.*, 1959, **38**, 573.

Serum Lactic Dehydrogenase

Q.—*What is the value of estimating the lactic dehydrogenase in clinical medicine? Does it give any more information than the serum glutamic pyruvic transaminase or serum glutamic oxaloacetic transaminase?*

A.—Estimation of serum lactic dehydrogenase (S.L.D.) activity is chiefly of value in the diagnosis of myocardial infarction. In this condition S.L.D. activity is almost invariably raised,[1] resembling the serum glutamic-oxaloacetic transaminase (S.G.O.T.), but not the serum glutamic-pyruvic transaminase (S.G.P.T.) in this respect.[2] After infarction S.L.D. elevation is more prolonged (average, 11 days) than S.G.O.T. elevation (average, 5 days),[3] and this may help establish a diagnosis in cases first seen some days after the infarct. Liver disease may be accompanied by S.L.D. elevation, but this is variable and unpredictable, and characteristic patterns of enzyme changes in the various disease categories, as exhibited by the transaminases,[4] are not shown.

In the examination of serous effusions the finding of effusion lactic dehydrogenase activity in excess of S.L.D. activity is claimed to indicate that the effusion is malignant.[5] Malignancy may cause increased S.L.D. activity and malignant involvement of the central nervous system increased cerebrospinal fluid lactic dehydrogenase activity.[6]

The interpretation of increased S.L.D. activity may be difficult because of the numerous diseases (cardiac, hepatic, muscular, renal, malignant, etc.) in which elevation may occur. Fractionation procedures designed to determine the tissue from which S.L.D. elevation has originated[6] are not suitable for routine laboratory use.

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5 Wróblewski, F., *Amer. J. med. Sci.*, 1957, **234**, 301.
6 —— Ross, C. and Gregory, K., *New Engl. J. Med.*, 1960, **263**, 531.

Spotting the Patient on Steroids

Q.—*What clinical signs should be apparent in a patient having hydrocortisone therapy?*

A.—By no means all patients receiving corticosteroids develop the features of "hypercortism" or Cushing's syndrome. However, the practised clinical eye can detect the "moon face" in the majority, though this is really the only immediately apparent physical sign. The presence of acne, hirsuties, oedema, and ecchymoses, especially on the legs, may give a lead, but are, of course, not specific. Likewise the presence of hypertension or glycosuria calls for direct questioning, particularly if the patient is known to suffer from a condition responsive to corticosteroids.

Chronic Furunculosis

Q.—*What is the treatment of chronic furunculosis of the neck, and should antibiotics, parenterally or locally, be given? If so, is continuous antibiotic treatment over several months advisable?*

A.—Chronic furunculosis of the nape of the neck may respond to radiation therapy in the form of dry heat, short-wave diathermy, ultraviolet irradiation, Grenz rays, or fractional doses of *x* rays. A local antiseptic such as

chlorhexidine diacetate 1 in 2,000, phenoxyethanol lotion 2%, chlorquinaldol ointment, or "naseptin cream," which contains neomycin and hexachlorophane, should be applied twice daily. Internally, sulphadimidine 0.5 g. three times daily after meals can be given over a period of 6 or 8 weeks. The nares and perineum and skin under the finger nails should be treated with the naseptin cream, and coat collars should be kept from contact with the neck by clean linen.

It is presumed that there is no other underlying disease or focus of infection and that the affection is simple furunculosis and not sycosis nuchae or one of the other more complicated cystic infections of the neck. A culture of the organisms and determination of their sensitivity reactions to antibiotics might indicate a more specific line of treatment locally or by mouth, but it is doubtful if this would be more effective than the measures indicated.

Culturing Trichomonas Vaginalis

Q.—*Can Trichomonas vaginalis be cultured in a laboratory? Is the technique practicable in a small laboratory, and is it worth while? If so, could you give some references?*

A.—Trichomonads have been cultured for many years, but it was with the advent of antibiotics that bacteria-free cultures became possible and cultural techniques used more widely. The two media commonly used in this country are those described by Stenton[1] and Fienberg and Whittington.[2] Apart from the necessity to add antibiotics and horse serum within a reasonable time before use, the technique presents no difficulty and can be used in any bacteriology laboratory. The question as to their value depends on what sort of investigation is planned. While direct examination is probably quite adequate for routine gynaecological out-patients, many workers have shown that culture of all specimens results in a higher number of positive cases. Whether the work involved is justified to diagnose minor infestations is, of course, questionable. However, cultural methods are essential if trichomonads are to be sought in males,[3 4] or treatment with trichomonacidal drugs assessed.[5]

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Drinking Absolute Alcohol

Q.—*I have a small number of patients who, on the grounds of economy, prefer to drink absolute alcohol either in coffee or combined with various fruit juices as a sort of liqueur. The average dose seems to be about one tablespoonful two or three times a day in coffee. Is there any harm likely if this practice is continued over a number of years?*

A.—It is unlikely that any more harm would come from this practice than might arise from the regular consumption of any alcoholic beverage of similar alcohol content to the final product. Indeed, a pharmacologist might well say that if one drinks because of the pleasant effects produced by alcohol then the proper thing to do is to take pure ethyl alcohol—i.e., absolute alcohol—suitably diluted. In this way one avoids any possible noxious effects from the essential oils, higher alcohols, and other substances which give most potent alcoholic beverages their characteristic flavour. Vodka, which is probably one of the most widely drunk spirits, is almost pure absolute alcohol. It is certainly a great deal safer to take alcohol in the form of absolute alcohol suitably diluted than to take some alcoholic drinks such as absinthe. The important point to remember, however, is that absolute alcohol is *pure* ethyl alcohol and that there is more alcohol in one tablespoonful of it than in an average glass of brandy. Because absolute alcohol is a colourless liquid like gin it is often dispensed in similar quantities with somewhat devastating effects.

NOTES AND COMMENTS

Phenothiazines and C.S.F. Protein.—Dr. M. D. ENOCH (Wickford, Essex) writes: In dealing with the question on phenothiazines and C.S.F. protein ("Any Questions?" January 28, p. 307) it was stated that there does not appear to be any information on the C.S.F. protein levels in patients who develop a Parkinsonian state while under treatment with phenothiazine drugs, other than the paper referred to by Smith.[1] Rightly, the questioner regards it as an important diagnostic pitfall, and in the answer it is stated that it would seem to be worth further investigation. In fact two papers relevant to this subject have been published.

In the first, Denzel[2] reports a series of 25 patients (mainly schizophrenics) on phenothiazine therapy, using 25 other mental patients as controls. In the phenothiazine therapy group six patients had increased protein (above 45 mg.), while in the control group eight patients had an increased protein. In this paper two further important points are made about these increased protein levels. Firstly, repeat spinal fluid examinations after patients were taken off medication revealed no positive correlation between the observed change and the drug withdrawal. Again—and this deals directly with the questioner's dilemma—the incidence of Parkinsonism did not appear to be related to the increase of protein. Only one patient of the abnormally high protein group of 14 patients had symptoms of Parkinsonism. In the second paper, Bruetsch[3] reported increased C.S.F. protein in schizophrenic patients not receiving any drugs.

Obviously the work done and published in this field is very limited. But from these it appears that the abnormal high protein levels in the C.S.F. are unspecific, and may, to a certain extent, be present in patients not on phenothiazine therapy. Therefore it cannot be assumed that the increased protein C.S.F. is the result of phenothiazine therapy.

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2 Denzel, H. A., ibid., 1959, **116**, 545.
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Dr. GEORGE X. TRIMBLE (Long Beach, California) writes: Reference is made to the question concerning a relationship between phenothiazine-induced Parkinsonism and elevated C.S.F. protein ("Any Questions?" January 28, p. 307), about which the expert stated there was a need for further data. Cain and Malcolm,[1] citing Smith's[2] finding of increased C.S.F. protein in patients receiving phenothiazines, found no C.S.F. abnormalities in the 12 patients who had spinal fluid examinations of a group of 39 patients with phenothiazine-induced extrapyramidal reactions. Spinal fluid examinations were done only in the first 12 patients of this group. Shev[3] describes a "curious dissociation of C.S.F. protein pattern and albumin-globulin ratio shifts" with subsequent reversal of changes in a patient with extrapyramidal symptoms due to triflupromazine, in whom spinal fluid electrophoretic patterns had been studied. Shaw and co-workers,[4] in describing a series of patients with severe seizures due to phenothiazine tranquillizers, reported normal C.S.F. findings in five patients, and an increase in the C.S.F. cell count in one. Other instances of severe Parkinsonian type neuromuscular reactions to phenothiazine drugs with normal C.S.F. findings have been described.[5 6]

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